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ANTIBIOTICS IN AUSTRALIAN PLANTS AND FUNGI.[1]

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OUR work on antibiotics commenced with investigations of locally isolated lower fungi and then extended to the larger fungi and the flowering plants. The lower fungi were grown in the laboratory in various culture media, but the larger fungi and the flowering plants were gathered in the field and the various parts extracted in a little water. These extracts and the fungal cultures were tested qualitatively for antibacterial activity by Heatley's cylinder-plate method[1] against *Staphylococcus aureus* and *Salmonella typhi*. This test may fail to detect some antibacterial substances if they are present only in small amount, or not readily diffusible or not effective against these test organisms. However, these limitations should not seriously handicap the test as a screen for our purpose of detecting possible new chemotherapeutic substances.

Lower Fungi.

Working with the lower fungi, we quickly found, as did others elsewhere at about the same time, that numerous naturally occurring Penicillia and Aspergilli produced antibacterial substances, many of which appeared to be penicillin. One of our groups of Penicillia produced an antibiotic which was active against a wide range of bacteria and appeared to be different from any substance recorded in the literature available to us at that time; we gave it the name penicidin. We isolated it in pure crystalline form, found that it was relatively toxic and its activity was suppressed slowly by serum, peptone and various other substances, and specifically and quickly by SH compounds. These compounds probably caused inactivation by direct chemical reaction; H_2S completely destroyed penicidin in aqueous or alcoholic solution without formation of a hydrosulphide. The characteristics of the substance did not recommend it for chemotherapy.[2][3][4][5][6][7][8] Meanwhile descriptions of claviformin,[9] patulin[10] and clavacin[11] appeared and these three were identified with each other.[12] Penicidin seemed very like them, and Sir Howard Florey kindly examined our material and reported it to be identical with the other three (personal communication).

Flowering Plants.

So far we have tested about 1200 flowering plants, mainly native to Australia,[13] and found about 50 active against *Staphylococcus aureus*. Very few were active also against *Salmonella typhi*.[14] Table I gives the active plants.

Work is proceeding on the antibiotics of *Drosera peltata*, which grows wild in the Adelaide hills, the berries of *Persoonia pinifolius*, a native of New South Wales not growing wild in South Australia, but kindly made available to us in a private wildflower garden, and some members of the Myrtaceæ, of which so many showed activity.

Drosera.—As the antibacterial activity resisted moderate heating, the plants were dried at 105° C., powdered and extracted under reflux with ethyl alcohol. Before extraction the Drosera powder, 1/10 in water, produced zones of inhibition of 25 millimetres and 10 millimetres against *Staphylococcus aureus* and *Salmonella typhi* respectively; after extraction for several hours no zones were detected. The alcoholic extract was evaporated to dryness and the residue at a dilution of 1/2000 produced a small inhibition zone against *Staphylococcus aureus* but not against *Salmonella typhi*, for which inhibition was just detectable at 1/1000. On heating the residue *in vacuo* an orange-yellow sublimate possessing strong antibacterial activity

[1] Read at a combined meeting of the Section of Pathology, Bacteriology, Biochemistry and Experimental Medicine and the Section of Public Health, Tuberculosis and Tropical Medicine at the Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

against *Staphylococcus aureus* and slight activity against *Salmonella typhi* appeared. Ether extraction of a steam distillate of the residue from the alcoholic extract also produced active yellow material, which was purified by chromatography to yield yellow crystals which at a dilution of 1/1000 gave inhibition zones of about 25·0 millimetres for *Staphylococcus aureus* and about 15·0 millimetres for *Salmonella typhi*. The crystals are being analysed and their range and mode of antibacterial action and their toxicity are under examination. Hydroxydroserone, a naphthaquinone isolated from *Drosera whittakeri* (Lugg *et alii*[15]) in the department of chemistry, University of Adelaide, was also tested for antibacterial action and at a dilution of 1/1000 gave an inhibition zone of about 12 millimetres with *Staphylococcus aureus* and a slight zone with *Salmonella typhi*. Besides this difference in activity the difference in colour of our crystals suggests that they are not hydroxydroserone.

TABLE I.
Australian Plants Showing Antibacterial Activity.
(a) Active Against *Staphylococcus aureus*.

Casuarinaceæ—
Casuarina Decaisneana, leaves.
Proteaceæ—
Grevillea Dallaceana, flowers.
Grevillea bipinnuatifida, leaves.
Lomatia silaifolia, flowers.
Cruciferæ—
Lepidium hyssopifolium, leaves.
Lepidium hyssopifolium, stems.
Lepidium hyssopifolium, roots.
Lepidium hyssopifolium, seeds.
Compositæ—
Olearia ramulosa, leaves.
Olearia ramulosa, seeds.
Pittosporaceæ—
Bursaria spinosa, leaves.
Myrtaceæ—
Agonis linearifolia, flowers.
Angophora intermedia, leaves.
Angophora intermedia, flowers.
Astartea fasciculata, leaves.
Astartea fasciculata, flowers.
Callistemon citrinus, leaves.
Callistemon citrinus, flowers.
Callistemon violaceæ, leaves.
Callistemon violaceæ, flowers.
Callistemon violaceæ, fruits.
Callistemon pallidus, leaves.
Callistemon pallidus, flowers.
Callistemon palludosus, flowers.
Callistemon phœniceus, flowers.
Callistemon rugulosus, fruits.
Callistemon rugulosus, leaves.
Callistemon salignus, flowers.
Callistemon viminalis, leaves.
Callistemon viminalis, flowers.
Calothamnus rupestris, leaves.
Calythrix glutinosa, leaves.
Chamælaucium uncinatum, flowers.
Chamælaucium axillare, flowers.
Chamælaucium megalopetalum, flowers.
Darwinia citriodora, leaves.
Darwinia citriodora, flowers.
Darwinia sp. (W.A.), flowers.
Darwinia collina, leaves.
Darwinia collina, flowers.
Eucalyptus fasciculata, flowers.
Eucalyptus leucoxylon, flowers.
Eucalyptus leucoxylon, fruit.
Eucalyptus leucoxylon var. *macrocarpa*, flowers.
Eucalyptus Lehmannii, leaves.
Eucalyptus Lehmannii, flowers.
Eucalyptus Lehmannii, fruit.
Eucalyptus megacarpa, flowers.
Eucalyptus sepulcralis, leaves.
Eucalyptus sepulcralis, flowers.
Leptospermum lævigatum, leaves.
Melaleuca hypericifolia, flowers.
Melaleuca platycalyx, leaves.
Melaleuca squarrosa, flowers.
Melaleuca violacea, leaves.
Melaleuca Wilsonii, flowers.
Regelia ciliata, leaves.
Regelia ciliata, flowers.
Regelia ciliata, fruits.
Regelia grandiflora, flowers.
Syncarpia laurifolia, leaves.
Thryptomene saxicola, leaves.
Verticordia Brownii, leaves.
Verticordia Brownii, flowers.
Verticordia monodelpha, flowers.
Verticordia plumosa, leaves.
Verticordia plumosa, flowers.

(b) Active Against *Staphylococcus aureus* and *Salmonella typhi*.
Proteaceæ:
Persoonia pinifolius, berries.
Persoonia salicina, berries.
Persoonia juniperina, berries.
Droseraceæ:
Drosera whittakeri, whole plant.
Drosera peltata, whole plant.

Persoonia.—Several hundredweight of *Persoonia pinifolius* berries were collected during August and September, when they were just ripening. Very young or very old berries showed little antibacterial activity, which occurred in the fleshy part only and was at its height in mature fruit changing from green to purple. Zones of inhibition with expressed juice were approximately 18 millimetres against *Staphylococcus aureus* and 26 millimetres against *Salmonella typhi*. After being dried and stored at room temperature for several months the berries still retained activity. The first batch was extracted in water and the extract preserved by freeze-drying. However, the antibacterial activity was relatively stable; watery extracts remained active at 2° C. or 18° C. for at least six months, and no significant reduction in activity followed exposure to buffers ranging between pH 2·2 and pH 10 for several hours or to temperatures between 60° and 100° C. for thirty minutes. The remainder of the berries were therefore dried at 60° to 105° C. and crushed to a fine powder in a ball-mill; the powder was moderately active and easily handled. The active substance was extracted from either dried extract or berry powder with methyl alcohol, which was then distilled off, and the residue, taken up in a little water, was extracted continuously for several hours with ethyl acetate. The ethyl acetate was removed by distillation, the residue was dissolved in a little ethyl alcohol, hot chloroform was added, and the precipitate which formed was filtered off; in the chloroform solution, which was very acid, the activity had been concentrated about 100 times. Analysis of this chloroform extract by paper partition chromatography revealed at least three acid spots, in one of which the activity was located and for which the Rf value was determined as 0·56. From watery extracts charcoal adsorbed some activity, which could be eluted with methyl alcohol.

Further purification of the Persoonia antibiotic was achieved by dry distillation of the residue from the chloroform extract, in which no nitrogen, sulphur or phosphorus was detected. The product was a pale yellow oil, which solidified to a white flaky mass at −10° C. and probably consisted of the antibiotic with only slight impurities. At a concentration of about 20 milligrammes per millilitre in water much of the oil remained undissolved, but inhibition zones of 17 and 21 millimetres were produced against *Staphylococcus aureus* and *Salmonella typhi* respectively. The zones with *Salmonella typhi* were distinct, with clear-cut edges, as compared with the hazy outlines of zones produced by all our cruder preparations. When sufficient highly purified antibiotic has been prepared it will be analysed and extensively investigated chemically and biologically. Partly purified extracts possessed a wide range of antibacterial activity inhibiting the growth of all organisms so far tested. Table II records the results of these tests. Results of cylinder plate assays indicated that over a fair range of concentrations the diameter of the zone of inhibition was proportional to the log of the concentration. For toxicity tests some residue from the chloroform extract was taken up in water and filtered through a Seitz EK pad. The greater part of the activity appeared in the filtrate, which was neutralized and inoculated in various amounts intraperitoneally into mice, all of which died. The smallest dose tested corresponded to 500 milligrammes per kilogram of body weight. As the material injected was only partly purified, the high toxicity might be due not to the antibiotic, but to an impurity. An inactive crystalline product was obtained during processing, but it was not lethal to a mouse in a dose of 20 milligrammes.

Myrtaceous Plants.—The majority of other active plants belonged, as Table I shows, to the Myrtaceæ, a family well represented among the Australian flora and including the gums or eucalypts. A few of these active plants, namely *Chamælaucium uncinatum* (Geraldton wax plant), *Darwinia citriodora* and *Agonis linearis*, were further investigated and the antibacterial activity located in the oil obtained from the flowers or leaves by steam distillation or ether extraction. The crude oil from the Geraldton wax flowers showed antibacterial action against *Mycobacterium phlei*, which suggested the possibility of activity against *Mycobacterium tuberculosis*. The oil was fractionated by distillation under reduced pressure in nitrogen. The active material occurred in the fraction boiling between 46° and 59° C. at 13 millimetres of mercury pressure, and representing only a small portion of the total volume; the greater part of the oil distilled over at lower temperatures. The crude oil inhibited the growth of *Staphylococcus aureus* at a dilution of 1/500 in nutrient broth, but as the active fraction was small, at most one-tenth of the total, an activity of at least 1/5000 may be expected for the active constituent. Cineol occurs in oils from eucalypts and other Myrtaceous plants; it has been considered partly responsible for their disinfectant action.[16][17][18] From Geraldton wax oil we were unable to obtain any crystalline material by low temperature treatment (about −60° C.) which caused eucalyptus oil containing 68% cineol to crystallize into a solid mass and tea-tree (*Melaleuca alternifolia*) oil containing a little cineol (about 5%) to become opaque, whitish and thickened. Cineol seems unlikely to be the active component of Geraldton wax oil.

Darwinia citriodora oil was obtained by steam distillation and ether extraction of crushed leaves and flowers. Crude oil showed some activity against *Salmonella typhi*. In watery extracts of the Darwinia and also of *Agonis linearis* flowers the antibacterial activity survived boiling under reflux for at least three hours. Ether extraction of Agonis flowers yielded an oil which, like that of *Darwinia citriodora*, showed activity against *Salmonella typhi* as well as *Staphylococcus aureus*. Our future work will aim at identifying the active constituents of the Australian oils, especially those which inhibit the Mycobacteria, and investigations of their antibiotic activity will then follow. Early work on Australian essential oils and their constituents determined phenol coefficients[16][17] which had little relation to possible chemotherapeutic activity.

Larger Fungi.

In a survey of about 350 species of larger fungi, mainly Basidiomycetes collected in South Australia, some promising material was found.[19] Eight fungi showed antibacterial activity against *Staphylococcus aureus*; they were *Amanita ochrophylla, Psalliota xanthoderma, Cortinarius rotundisporus* and five new members of *Cortinarius*, of which two have subsequently been described under the names *Cortinarius austro-evernius* (closely related to *rotundisporus*) and *Cortinarius basirubescens*.[20] Extracts from the first three and from *Cortinarius austro-evernius* and an undescribed *Cortinarius* also inhibited *Salmonella typhi*. Furthermore, *Cortinarius rotundisporus* or *austro-evernius* and *Psalliota xanthoderma* inhibited *Mycobacterium phlei*.[21]

Cortinarius rotundisporus or *austro-evernius*.—This toadstool grows in small numbers in the Adelaide hills and may be collected about midwinter. Some variations appeared among our collections and the material extracted corresponded more closely to *austro-evernius* than to *rotundisporus* (Harris, personal communication). The antibacterial activity of crude extracts was fairly resistant and changed little during six months at 2° to 4° C., nor was it obviously decreased by moderate heating, by limited exposure to acid or alkaline conditions or by mixing with serum or thioglycollate. Chloroform extraction produced a very small amount of partly purified antibiotic which strongly inhibited *Staphylococcus aureus, Salmonella typhi* and *Mycobacterium phlei* in nutrient broth and toxicity did not seem very high. Possibly other active members of *Cortinarius*, affecting only *Staphylococcus aureus* in our preliminary test, may contain an antibiotic similar to *rotundisporus* or *austro-evernius* but in lower concentration. The inhibition zones of crude extracts against *Staphylococcus aureus* were so small as to suggest that activity against *Salmonella typhi* would not be apparent. The stability of the antibacterial substance of *Cortinarius austro-evernius* was emphasized by the detection of good activity in dried specimens over a year old. A fuller investigation of this interesting *Cortinarius* group, of which several inactive members have also been found, will be carried out in the next season.

Psalliota xanthoderma.—This edible mushroom was gathered from country districts widely separated throughout South Australia and from city parks and suburban gardens in Adelaide. Through the summer and early autumn it came up after heavy rain. Slight variations appeared among the specimens of *Psalliota* identified as *xanthoderma*, but all showed an iodine-brown stain when cut or scraped, and all showed the typical antibacterial activity which was greater against *Salmonella typhi* than against *Staphylococcus aureus*. Cleland and Harris[20] suggest calling this type "variety *antibioticus*". Water extracted the antibacterial substance from minced mushroom; twelve treatments on the same mushroom pulp failed to extract all activity, which fell off, however, in the later extractions; in the earlier extractions typical results for the zones of inhibition of *Staphylococcus aureus* and *Salmonella typhi* were 25 millimetres and 27 millimetres respectively. The mushrooms and their crude extracts retained activity for no more than two weeks at 2° C., but after precipitation at pH 3 followed by Seitz filtration and return to pH 7 crude extracts remained active at 2° C. for a month or longer. No obvious improvement in stability of activity followed preliminary treatment of the mushroom with hot ethyl alcohol to destroy enzymes possibly causing inactivation. Freeze-drying successfully preserved filtered extracts and minced mushroom. The powder produced from the extract was hygroscopic, but retained activity for at least two years when stored at 2° C. with an air-tight seal. Under the same conditions the dried minced mushroom also retained good activity for at least six months. Several hundredweight of mushrooms, available in the season, were processed, freeze-dried and stored. Thus material was available for the whole year, in spite of the seasonal occurrence of the Psalliota and its rapid loss of activity on storage.

Purification or concentration of the active material has proved difficult. From dried extract or dried minced mushroom, methyl, ethyl, butyl or amyl alcohol, ether, chloroform or ethyl acetate extracted a little of the antibiotic. From watery extracts the activity was dialysable through "Cellophane"; it could also be adsorbed on charcoal, from which a small amount could be eluted with methyl or ethyl alcohol. The activity extractable into methyl alcohol seemed more stable to heat than that of the crude watery solutions. Exposure of these solutions to pH 9 or pH 2 for 20 minutes had little effect, but heating to 100° C. at pH 9, 7 or 2 for twenty minutes greatly reduced activity. Removal of the solvent from the methyl alcohol extract left a yellowish residue, the greater part of which dissolved in water in which the activity withstood exposure to a temperature of 100° C. for twenty minutes at pH 10, 7 or 3. Chromatography of extracts with the use of alumina activated in various ways, silica gel, talc and French chalk resulted in some purification but no concentration. In none of the columns was the activity confined to a definite band, and frequently it appeared in the percolate. Filtration through membranes of pore sizes 400$\mu\mu$, 200$\mu\mu$ and 60$\mu\mu$ caused no diminution in activity.

Recently we obtained a better source of active material by growing a culture of the mycelium of *Psalliota xanthoderma* from young mushrooms. On oatmeal or malt extract agar growth appeared at 22° C. in about two weeks; subcultures grew well, but slowly. The cultured mycelium when touched changed to a bright orange colour similar to that seen in the mushroom. It contained good antibacterial activity, which was not detected in the culture medium. Water, ether or ethyl acetate extracted activity from the mycelium; an extract approximately 1/100 in water gave inhibition zones of 18 millimetres for *Staphylococcus aureus* and 23 millimetres for *Salmonella typhi*. As the mycelium contained at least 80% of water, the active substance must be present in a concentration much less than 1/100 and, judging by the zone sizes, should be capable of producing antibacterial titres of the order of 1/100,000 at least. Isolation of the antibiotic from the mycelium should prove easier than from the mushrooms. In preliminary exploration of an ether extraction method the mycelium was harvested aseptically from cultures which, on reincubation, rapidly yielded more growth. At least four such harvests could be obtained from a single culture. This improvement in amount and rate of growth on media which has already supported growth suggested that some stimulating substance, previously absent or present in inadequate amount, had been produced by the first crop of mycelium and absorbed into the medium which had obviously darkened at the first harvest. However, the enhancement might be due to the large and well-spread inoculation resulting during the harvesting. Subsequently fresh culture medium was inoculated heavily with chopped mycelium, but showed little improvement in growth. This result suggested that the deficiency probably lay in the medium, upon which we are working for its improvement. The harvested mycelium was extracted with ether and yielded a brown oily material with activity against *Salmonella typhi* up to a dilution of 1/2000. This material was still very impure, but adsorption treatment or chromatography of large quantities of ether or other solutions will, we hope, result in the ultimate purification of the antibacterial substance. The concentration of antibiotic could be followed from the size of the zone of

inhibition produced in twenty-four hours at 37° C. on plates prepared by a standard technique in which *Salmonella typhi* or *Staphylococcus aureus* was used. As a standard of reference small amounts of a solution of powdered extract were freeze-dried and stored at −20° C. Solutions of this material retained activity unaltered for at least six weeks at −20° C. After this period a fresh standard was prepared from a previously unopened ampoule. Zone size appeared proportional to the log of the concentration over a wider range for *Staphylococcus aureus* than for *Salmonella typhi* and zones of 20 to 25 millimetres for *Staphylococcus aureus* and 22 to 24 millimetres for *Salmonella typhi* seemed suitable for assay. The standard diluted 1/10 produced such zones and should be included at this concentration in some plates of all assays.

Under aerobic or anaerobic conditions and in a variety of culture media, including Brewer's thioglycollate medium,

TABLE II.

Sensitivity of Various Bacteria to Persoonia and Psalliota Antibiotics.[1]

Organism.	Antibiotic.	
	Persoonia.	Psalliota.
Mycobacterium—		
Myco. phlei	+	+
Myco. tuberculosis (human type)	Not done	+
Corynebacterium—		
C. diphtheriæ mitis	+	±
C. diphtheriæ intermedius	+	±
C. ovis	+	+
C. equi	+	+
C. hofmanni	+	+
C. murium	+	+
Brucella—		
Br. abortus	+	+
Br. melitensis	+	+
Br. bronchisepta	+	+
Bacillus—		
B. subtilis	+	+
B. mycoides	+	+
B. anthracis	+	−
Micrococcus and Sarcina (three strains)	+	+
Streptococcus—		
Hæmolytic strep. (Rammelkamp)	+	+
Hæmolytic strep. (Group A)	+	+
Strep. agalactiæ (Group B)	+	+
Strep. fæcalis	+	+
Strep. viridans	+	−
Neisseria—		
N. catarrhalis	+	+
Pasteurella—		
P. pestis	+	+
P. muriseptica	+	+
P. aviseptica	+	+
P. pseudotuberculosis	+	+
Lactobacillus—		
L. casei	+	+
L. bulgaricus	+	+
Salmonella—		
S. typhi[2]	+	+
S. typhi (16 strains including phage types A, D_2, C and F_2)	+	+
S. paratyphi B	+	+
S. choleræ-suis	+	+
S. pullorum	+	+
S. blegdam	+	−
S. paratyphi A	+	−
S. enteritidis	+	−
S. ballerup	+	−
S. typhi-murium	+	−
S. bovis-morbificans	+	−
S. reading	+	+
S. poona	+	+
S. senftenberg	+	+
S. aberdeen	+	−
S. newington	+	−
S. adelaide	+	−
S. hvittingfoss	+	−
S. cerro	+	−
S. moscow	+	−
S. bonariensis	+	−
S. san-diego	+	−
S. abortus-equi	+	−
S. cambridge	+	−
S. oslo	+	−
S. litchfield	+	−
S. derby	+	−

[1] To test qualitatively for sensitivity heavy streaks of the organisms were arranged radially around a central cylinder on a nutrient agar or blood agar plate. The antibiotic was added to the cylinder and the plate incubated at 37° C. for 24 hours. In Table II " + " indicates failure to grow within about three millimetres or more of the central cylinder and " − " indicates growth right up to the cylinder. The Clostridia were tested in Brewer's medium containing the antibiotic material in a dilution of about 1/160; " + " indicates failure to grow and " − " indicates growth. The results recorded were derived from several tests on each organism.

TABLE II.—*Continued.*

Sensitivity of Various Bacteria to Persoonia and Psalliota Antibiotics.—Continued.

Organism.	Antibiotic.	
	Persoonia.	Psalliota.
Dysentery bacilli—		
Bact. dysenteriæ Shiga	+	+
Bact. dysenteriæ Flexner	+	+
Bact. sonnei	+	+
Z_4 paracolons (Arizona group)—		
S. arizona	+	+
S. hudson	+	+
NJ 4	+	+
PC 36608	+	+
S. atherton	+	−
S. waycross	+	−
Coliforms—		
Bact. coli I	+	+
Bact. friedlanderi	+	+
Bact. aerogenes	+	−
Pseudomonas—		
Ps. pyocyanea	+	−
Chromobacterium—		
Chr. prodigiosum	+	+
Staphylococcus—		
Staph. aureus B 313[2]	+	+
Staph. aureus (human origin)	+	+
Staph. aureus (bovine origin)	+	+
Staph. albus	+	+
Proteus—		
P. morgani	+	+
P. XK	+	+
P. X19	+	+
Clostridium—		
Cl. sporogenes	+	−
Cl. tetani	+	+
Cl. botulinum Type B	+	+
Cl. septique	+	+

[2] These strains are used in routine testing.

tryptic digest broth and blood agar the Psalliota antibiotic possessed a wide range of antibacterial activity, smaller, however, than that of Persoonia antibiotic, which was also active under all conditions tested for Psalliota. Table II gives the results of sensitivity tests.

Against a strain of *Mycobacterium tuberculosis* of the human type isolated in our laboratory and regularly found infective to guinea-pigs in a dose of 0·001 milligramme moist weight, Psalliota powder two years old was active in physiological saline or Dubos's modification[22] of Kirchner's medium. From mixtures of inhibitory concentrations of Psalliota antibiotic and tubercle bacilli in physiological saline at room temperature subcultures after twenty-four hours into glycerol serum broth and onto egg media yielded no growth. In "Tween 80" medium (0·1%) after four days at 37° C. the control showed heavy flocculant growth, but no floccules were visible in the tubes containing Psalliota powder 1/4 to 1/64; at 1/128 and 1/256 growth appeared much lighter than that of the control. The same material in nutrient broth with and without "Tween 80" (0·1%) inhibited *Staphylococcus aureus* and *Salmonella typhi* at dilutions of 1/40 and 1/160 respectively. Thus "Tween 80" seemed not to interfere with the antibacterial action of Psalliota antibiotic against these organisms. It may enhance the action of other antibiotics on tubercle bacilli,[23] but our tests in saline suggested that it was not responsible for their sensitivity to Psalliota antibiotic, which probably killed them in the "Tween" medium within twenty-four hours. Prolonged bacteriostatic action seemed unlikely, as the antibiotic rapidly lost its potency at 37° C. Unlike streptomycin,[24] Psalliota antibiotic apparently killed the organism in the presence or absence of culture media. Preliminary tests indicated that Psalliota antibiotic would probably prove ineffectual against bacterial viruses. Phage adapted to *Salmonella blegdam* produced lysis of the organism in nutrient broth containing Psalliota powder 1/40, the greatest concentration in which *Salmonella blegdam* would grow. More extensive tests, including typhoid, paratyphoid B and staphylococcal phages are being undertaken.

Sensitive bacteria may readily be adapted *in vitro* to withstand greatly increased concentrations of penicillin or streptomycin. We quickly trained *Staphylococcus aureus*

to become thousands of times more resistant and *Salmonella typhi* hundreds of times more resistant to streptomycin. These adapted strains and cultures of *Staphylococcus aureus* naturally or artificially rendered resistant to penicillin were still sensitive to Psalliota antibiotic. Using similar methods we tried to adapt *Staphylococcus aureus*, *Salmonella typhi* and *Neisseria catarrhalis* to Psalliota antibiotic, but adaptation seemed not to occur readily. Little alteration in sensitivity appeared in any organism, although the staphylococci showed morphological changes like those observed during penicillin adaptation and individual cocci grew very large.

Oxalated human blood, blood serum or lysed human red blood cells produced no detectable effect on the activity of the Psalliota antibiotic, nor did the antibiotic affect the blood. The toxicity of crude active extracts of Psalliota was low and seemed to be mainly due to the potassium content. In mice injection intraperitoneally of a solution of powdered extract (inhibition zones at 1/10 approximately 25 millimetres *Staphylococcus aureus*, 27 millimetres *Salmonella typhi*) corresponding to about 4·0 grammes per kilogram body weight caused some discomfort and a few mice died in about two days; a dose corresponding to about 6·0 grammes per kilogram killed the majority of mice injected. The latter dose contained the equivalent of about 1·0 gramme per kilogram of potassium chloride. When purer preparations of the antibiotic are available toxicity tests will be repeated.

Discussion.

New chemotherapeutic agents may be discovered by the empirical or the rational approach. The rational approach demands a knowledge of the fundamental principles of the modes of action of chemotherapeutic substances. Unfortunately for the immediate rational development of chemotherapeutic agents, few such principles have so far been established. Fildes[25] in England and Albert[26] in Australia advocated the rational approach to research in chemotherapy. Fildes's theory stated that antibacterial action depended upon interference with an essential metabolite, often by competition for an enzyme associated with it. Fildes suggested that research in chemotherapy might well be directed to the development of metabolite analogues, modifications of known essential metabolites which fitted the same enzyme but were devoid of essential metabolic activity. Many of these metabolite analogues were prepared and showed antibacterial activity.[27] Albert conducted a large-scale investigation of the acridine compounds with a view to discovering principles and not necessarily new chemotherapeutic agents. The activity of the acridines was found proportional to the degree of cationic ionization, and competition between them and hydrogen ions was considered the basis of the antibacterial action. Another mode of action suggested for chelating compounds such as 8-hydroxyquinoline was by removal of essential trace metals, such as cobalt. Based on such principles, Albert considered that man might produce molecules "tailor-made" to suit his purpose.

But we are far from the ideal of the tailor-made molecule, and therefore empirical search is still important in the discovery of new chemotherapeutic agents and through them of new principles of action. The empirical method has so far yielded the most valuable chemotherapeutic agents against bacterial infections, the sulphonamides and penicillin. The great success of penicillin focused attention on the antibiotics among which, as products of biological activity and not of man's inventiveness, molecular types as yet undreamed of may be found and the horizons of chemotherapy be extended. Therefore, we are continuing our empirical search among the Australian plants and fungi. Similar sources have also been studied elsewhere. Some representative investigations are those of Wilkins, who examined numerous fungi, including Basidiomycetes[29][30][31] and considers, as we do, that the group is most interesting; Osborn,[32] who examined a wide range of flowering plants; Heatley[33] and Cavallito and colleagues,[34][35] who isolated and examined antibacterial substances from various plants. Apart from penicillin and streptomycin, few antibiotics of the many discovered have chemotherapeutic promise. Until we have further studied the antibacterial crystals of Drosera and oils from Myrtaceous plants we hesitate to predict possible uses. Our Persoonia antibiotic may prove too toxic for chemotherapy, except perhaps for local application, where its ability to inhibit *Pseudomonas pyocyanea* and many common bacteria may be useful. The Psalliota antibiotic seems more likely to be valuable chemotherapeutically. It is active against *Mycobacterium tuberculosis* and numerous other bacteria, including strains relatively insensitive to penicillin or streptomycin. The activity seems little affected by blood, and bacteria do not readily adapt themselves to it. Crude preparations have low toxicity. However, it is difficult to isolate from mushrooms and we hope to purify it from cultivated mycelium. In the Salmonella and other groups it shows a selective action, the basis of which is under investigation and may expose unsuspected differences between members. The Cortinarius antibiotics appear relatively harmless, not easily inactivated and effective against acid-fast and Gram-positive and negative organisms. We plan to investigate them and the antibiotic of *Amanita ochrophylla* more fully next season.

Even if none of our substances finds an application in chemotherapy, a study of their mode of action may reveal new principles. Preliminary investigations suggest that the activity of Psalliota antibiotic is unlikely to be due to H_2O_2 production. Material prepared, as described for notatin,[36][37] showed no activity in glucose or other media. Red blood cells whole or lysed or SH compound had little effect on activity, which appeared in protein digest as well as simple media. The discovery of specific suppressors may aid in unravelling the mode of action. None have yet been found, but our crude preparations may contain them undetected. Even after moderate heating these materials strongly stimulate the growth of *Staphylococcus aureus*. The ready production of resistance in certain bacteria to penicillin or streptomycin but not to Psalliota antibiotic and the susceptibility of these resistant strains to our antibiotic suggest that its mode of action differs markedly from that of streptomycin or penicillin. With purer preparations of our antibiotics becoming available, the study of their modes of action will be greatly facilitated.

This report deals with work in progress and necessarily, therefore, contains much that is incomplete. For these shortcomings I beg your tolerance and hope that in time we will provide the missing information.

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STREPTOMYCIN, POLYMYXIN AND CHLOROMYCETIN.[1]

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Streptomycin.

THE production of streptomycin by the fungus *Streptomyces griseus* was reported by Waksman and his colleagues early in 1944. In broad outline, current methods of streptomycin production are as follows. The mould is grown in submerged, aerated, agitated culture in large fermenters, in a simple medium containing yeast or meat extract, glucose, and small quantities of inorganic salts. The streptomycin in the cell-free harvest fluid is adsorbed on activated carbon at a pH around neutrality, and is subsequently eluted from the carbon by an acid, water and organic solvent mixture at a pH of approximately 2·0. Streptomycin is insoluble in high concentrations of organic solvents, and by the addition of further solvent to the eluate, streptomycin is precipitated. By such methods, a product of about 50% purity can be obtained. Further purification of this material is effected by the use of adsorbents other than carbon, or by conversion to the insoluble streptomycin helianthate, from which streptomycin hydrochloride, streptomycin sulphate or the calcium chloride complex—all of high purity—can be obtained. The product is dispensed in aqueous solution in the final container, in which it is vacuum-dried from the frozen state.

The various stages of production are controlled by a variety of assay procedures both biological and chemical. Before release for use, the commercial product is tested for potency, sterility, dryness, clarity and pH of the product on reconstitution, and for freedom from histamine-like and pyrogenic substances and from substances toxic to mice on intravenous injection.

Streptomycin is an organic base, fairly stable to heat and pH changes, and showing its greatest antibacterial effect in a slightly alkaline medium. It has a fairly wide antibacterial spectrum against Gram-positive and Gram-negative organisms and to the tubercle bacillus, but considerable variation of susceptibility may occur among strains of the same species.

It is of interest that the existence of at least two chemically distinct forms of streptomycin has been established. However, in view of the experience gained in the recognition of the various penicillin types—such as penicillins *F*, *G*, *X* and *K*—with their different antibacterial, pharmacological and therapeutic characteristics, there would appear to be little danger in the case of streptomycin that anything but a well-proofed and therapeutically active product will be made available for clinical use.

[1] Read at a meeting of the Section of Pathology, Bacteriology, Biochemistry and Experimental Medicine and the Section of Public Health, Tuberculosis and Tropical Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

Two characteristics of streptomycin, militating against its value as a therapeutic agent, are the ease with which many organisms rapidly acquire a high degree of tolerance for the drug, and its toxicity to man, especially in relation to the production of vestibular dysfunction. Because of these characteristics, careful judgement in the matter of dosage schedule and of the time of exhibition of streptomycin in relation to the general management of a patient is often necessary to ensure maximal therapeutic with minimal toxic effect.

Current views on the place of streptomycin in the treatment of tuberculosis have been referred to at previous meetings, and the subject will be discussed further in a subsequent paper during this meeting.

The therapeutic value of streptomycin in diseases other than tuberculosis may be stated as follows:

1. Streptomycin has a definite place with sulphadiazine and specific rabbit antiserum in the treatment of *Hæmophilus influenzæ* meningitis.

2. In infections of the urinary tract with Gram-negative organisms, streptomycin has been found effective in a worth-while proportion of cases. It is desirable to render the urine alkaline during treatment, with a view to enhancing the antibacterial action of the drug and possibly reducing the tendency to the development of streptomycin-resistant strains.

3. Trials of streptomycin in pertussis have shown it to be of some value.

4. Streptomycin, applied topically, appears to be the best available agent for the prophylaxis or treatment of wound infections with Gram-negative organisms.

5. Streptomycin appears to be the best chemotherapeutic agent available for acute undulant fever. Encouraging reports have been made of the value of combined treatment with streptomycin and sulphadiazine in chronic brucellosis.

6. In small doses, streptomycin is an extremely effective therapeutic agent in tularæmia.

7. A small number of cases of bacterial endocarditis has been reported, in which the infecting organism was penicillin-resistant, and in which the condition has been successfully treated with streptomycin.

Streptomycin has considerable value in the treatment of Friedländer's bacillus pneumonia.

9. Preliminary reports indicate that streptomycin will be of value in the treatment of plague.

10. It is probable that streptomycin will prove useful in the treatment of peritonitis, and in the general management of surgical conditions of the (large) bowel.

The problems of drug-fastness, and, when large doses or prolonged treatment has been given, of toxic effects of streptomycin, have been encountered in most of the diseases mentioned above, and, in some cases, the development of streptomycin-resistant strains has apparently accounted for failure of therapy.

Let me summarize my remarks on streptomycin by saying that it is a valuable chemotherapeutic agent, and that careful clinical judgement and laboratory supervision are often required to ensure that the full therapeutic potentialities of the drug are realized and that the hazards of streptomycin therapy do not outweigh the probable therapeutic effect.

Polymyxin.

About the middle of last year the production of an antibiotic from a bacterium *Bacillus polymyxa* was reported independently by two groups of American workers—Benedict and Langlykke, of the Northern Regional Research Laboratory, Peoria, Illinois, and somewhat later, Stansly, Shepherd and White, of the American Cyanamid Company, Connecticut. This second group proposed the name polymyxin for the antibiotic studied by them. About the same time, Ainsworth, Brown and Brownlee, of the Wellcome Physiological Research Laboratories, Kent, reported the production of an antibiotic, called by them aerosporin, from *Bacillus aerosporus*, which is closely related to *Bacillus polymyxa*. It appears that polymyxin and aerosporin are similar, but not identical, and are in fact two of a number of antibiotics produced by different strains of an ill-defined group of aerobic, Gram-variable, spore-bearing bacilli. They are predominantly active against Gram-negative bacilli, including the colon-typhoid-dysentery organisms, the cholera vibrio and the hæmophilus group. Although encouraging results of the therapeutic action of polymyxin and aerosporin in experimental animal infections have been described, there have been no reports, of which I am aware, establishing the value of these antibiotics in human disease. In the case of aerosporin, toxic effects, the most serious of which was renal damage, occurred with early batches available for trial; but these effects may have been associated with impurities in the preparation. A report by Swift claiming some value for aerosporin in pertussis appears in *The Lancet* of January 24, 1948, and references to encouraging results with polymyxin in trials in human disease appear in *The Journal of the American Medical Association* of April 24, 1948. Investigations of antibiotics produced by other members of this group of bacteria are being continued and there are indications that they may yield a useful non-toxic antibiotic.

Chloromycetin.

The third antibiotic with which I am concerned in this paper is chloromycetin. The discovery of chloromycetin was published in October of last year by Ehrlich and his colleagues, of the Parke, Davis Research Laboratories, Detroit, and Burkholder, of the Yale University. The organism which these workers found to produce chloromycetin is a Streptomyces species isolated from a soil sample collected in a mulched field near Caracas, Venezuela, and the name *Streptomyces venezuelæ* has been proposed for the organism. The name chloromycetin presumably derives from the fact that the chloromycetin molecule contains non-ionic chlorine, and from its production by a fungus. In January of this year Carter, Gottlieb and Anderson, of the Illinois University, published an account of the isolation from a local soil sample of a strain, probably identical with *Streptomyces venezuelæ*, which also produces chloromycetin. Methods of chloromycetin production in submerged culture, extraction from the culture broth and final purification have been developed by Parke, Davis and Company in America.

Chloromycetin is a neutral compound and is much more stable to heat or pH changes than penicillin or streptomycin. Satisfactory blood concentrations of chloromycetin follow oral administration; only a small percentage of the chloromycetin administered is recoverable from the urine.

Reports to date of the in-vitro antibacterial activity of chloromycetin indicate that it is moderately active against Gram-positive bacteria and the tubercle bacillus, and that it is highly active against the strains of the following Gram-negative organisms which have been tested: the typhoid and paratyphoid B bacilli; the Sonne dysentery bacillus; strains of the coli-aerogenes group; *Hæmophilus pertussis*; *Brucella abortus*, *Brucella melitensis*, *Brucella suis* and *Brucella tularensis*; Friedländer's bacillus; *Proteus vulgaris*.

Of at least equal, if not greater, interest than the antibacterial activity of chloromycetin is its antirickettsial activity. It has given excellent results in the treatment of experimental infections of chick embryos with the causative rickettsiæ of scrub typhus, classical typhus, murine typhus and Rocky Mountain spotted fever, and its efficacy in experimental scrub typhus in mice has been established. Chloromycetin also has significant therapeutic activity in chick embryos and mice infected with viruses of the psittacosis and *lymphogranuloma venereum* group. Viruses against which it has not been found effective in experimental infections are the influenza *A* virus and variola virus.

In March and April, 1948, a controlled study of the value of chloromycetin in scrub typhus occurring in the Kuala Lumpur district of Malaya was carried out by American workers, under Dr. Smadel, of the United States Army Medical Research Department, and Dr. Lewthwaite and Dr. Savoor, of the Kuala Lumpur Institute for Medical Research. In a series of 25 cases treatment with chloromycetin was begun, on the average, on the sixth day of the disease. The average duration of fever after the

commencement of treatment was thirty-one hours. In the control group of 12 cases the average duration of fever was eighteen days. In the treated group the rapid defervescence was accompanied by an equally dramatic improvement in the general condition of the patients. No complications or deaths occurred among the 25 treated patients; in the control group of 12, parotitis in one case and pneumonia in another occurred as complications, and there was one fatal case. In the later stages the trial dosage of chloromycetin was simplified to the oral administration over a period of twenty-four hours of approximately six grammes. No effects suggestive of toxicity of chloromycetin in the doses used were observed.

It is obvious that, in view of its proven efficacy in scrub typhus and of its wide range of antibacterial, antirickettsial and, to a less extent, antiviral action *in vitro* or in experimental infections, the results of trials of chloromycetin in a number of important human diseases will be awaited with great interest.

RECENT DEVELOPMENTS IN UROLOGY.[1]

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INFECTIONS OF THE URINARY TRACT.

Pyelitis and Pyelonephritis.

MOST of the conditions diagnosed here under the name of acute pyelitis are really cases of pyelonephritis. A temperature of 103° F. with a chill does not result from an infection of a small surface lined by pseudostratified epithelium. The kidney parenchyma is also involved and the term pyelonephritis should be used. As you know, in most of these cases the patients respond after a short severe illness to suitable treatment, but we have not laid enough stress here on the possible sequel of chronic pyelonephritis which may follow the acute disease, especially the so-called pyelitis of pregnancy. It is most important that these patients should be followed up and their urine examined microscopically for pus and organisms during their convalescence, while the infection can still be dealt with and before the chronic condition becomes established.

Pathologically, chronic pyelonephritis is a chronic or recurrent inflammation of the interstitial tissue of the kidney with progressive destruction of functional renal elements and fibrosis and scarring of kidney and pelvis. Once established, this is a serious and intractable disease. Of 176 patients followed by Nesbit, only 2·3% were cured by treatment, although 30% were improved.[(4)] It is one of the commonest renal causes of hypertension. Death occurs from cardio-vascular or renal failure.

In any case of urinary tract infection, then, in which infection persists after treatment or in which infection recurs, the patient must be first subjected to full investigation of the urinary tract to uncover any predisposing pathological cause. If any abnormality is found, this must be corrected, by surgery if necessary, and treatment must be instituted with the object of clearing the infection right up.

The most effective urinary antiseptics are the sulphonamides, penicillin and streptomycin. The last-mentioned drug is now freely used in the United States and has proved to be effective in many cases of urinary tract infection which has not responded to sulphonamides or penicillin. The usual dose is one to two grammes per day, divided into six four-hourly injections, and the drug is continued usually for not more than three to five days. Streptomycin has a rapid lethal effect on sensitive organisms, and if it is not effective in this time it is not likely to be of use. Used in this way and for a few days only, the drug is safe and the incidence of toxic symptoms is negligible.

However, there are still organisms which do not respond to any of these antiseptics. Among the most troublesome at present are some strains of *Proteus vulgaris* and of *Aerobacter aerogenes* (*Bacillus lactis aerogenes*). Unless special bacteriological methods are used this latter organism may be confused with the *Bacillus coli* group, and it probably accounts for some of the resistant coliform infections we meet here.

Urinary Tuberculosis.

Streptomycin is proving a valuable adjunct in the management of cases of tuberculosis of the urinary tract. The drug is particularly useful in cleaning up residual infection in ureter and bladder after nephrectomy. Most surgeons are, in addition, using it before operation to try to sterilize the kidney at least temporarily and prevent risk of disseminating the disease at operation.

The drug is given in doses of from 1·5 to 2·0 grammes daily for periods up to ninety days. The higher doses result in severe and permanent vestibular nerve damage in nearly all cases, but this is regarded as a price the patient has to pay to be rid of his disease. "Moogrol" and sometimes "Promizole" are given in conjunction with streptomycin and are believed to increase the efficacy of this drug.[(7)]

With streptomycin therapy some otherwise hopeless subjects of bilateral disease have shown remarkable improvement with disappearance of the organism from the urine, at least temporarily. One patient I saw in Nesbit's wards had practically the whole of his genito-urinary tract infected with the disease. Both kidneys, both ureters, both epididymes, bladder and urethra were diseased, and on top of that he had developed tuberculous meningitis. After a prolonged course of streptomycin therapy he was, when I saw him, apparently well and was gaining weight; no tubercle bacilli could be isolated from the nephrostomy opening draining his sole remaining kidney, and his cerebro-spinal fluid had returned to normal.

Nesbit is now trying a sixty-day period of treatment with streptomycin, "Moogrol" and "Promizole", and is reviewing the position. If investigations then show that healing has occurred, he intends to continue this treatment for another thirty days and try to avoid surgery alogether. He points out that the results of surgery for so-called unilateral tuberculosis are none too good, for in only 50% of cases does the patient survive five years or more. The doses of the various drugs he is using at present are as follows: streptomycin, two grammes daily for ninety days; "Moogrol", three millilitres given intramuscularly each day during the period of streptomycin therapy; and "Promizole", four to six grammes daily over the period of streptomycin therapy and two to four grammes daily thereafter to complete a total period of six months. This last drug may cause agranulocytosis and the white blood cell count has to be watched.

Nesbit's present therapy is experimental and it is going to take some time for streptomycin to find its proper place in the management of this condition. It certainly seems reasonable to treat with streptomycin the subject of so-called "tuberculous bacilluria" without demonstrable lesion, but in other cases of demonstrable unilateral disease most surgeons use the drug only as an adjunct to surgical treatment.

One unexpected complication of streptomycin therapy reported by O'Conor, of which it may be well to beware, is the fact that lesions of the ureter may heal rapidly and suddenly produce a stricture with complete obstruction to urinary flow from that kidney.

Tumours of the Testicle.

Lloyd C. Lewis has studied and produced a report on 250 cases of testicular tumour.[(8)] The classification he uses is more complex than the simple one to which we are accustomed and follows that worked out by N. B. Friedman and others who studied more than 900 tumours in the American army.[(9)]

In essence Lewis has related histology to radiosensitivity and planned treatment accordingly.

[1] Read at a meeting of the South Australian Branch of the British Medical Association on December 15, 1948.

Seminoma accounted for about 40% of his cases. These tumours are very radiosensitive. A group of carcinomata is distinguished which is only moderately radiosensitive. Tumours containing trophoblastic tissues are affected only by very large doses of X rays, and mature teratomatous tissue needs such large doses that X-ray therapy is impracticable.

The treatment recommended for testicular tumours then is as follows. The testis is removed via an inguinal incision and a section is examined. If the tumour is a seminoma this completes the operation and the patient is now given deep X-ray therapy to the appropriate lymph glandular area. In the case of other types of tumour a radical operation is now proceeded with. This entails a block dissection of the lymph-bearing tissue from the point of section of the cord up to the renal vessels, and from the iliac vessels and aorta medially to the spermatic vessels laterally. This extension of the operation may be carried out after study of a frozen section, or perhaps better several days later after a careful study of the whole of the tumour. In the case of the more sensitive tumours this is then followed by a course of deep X-ray therapy.

This plan of treatment appears to have gained wide acceptance in the United States. Lewis himself prefers a radical dissection in all cases but admits that it is probably not necessary in the case of seminomata.

Urinary Calculi.

There have been only minor improvements in therapy for urinary calculi. Patients with bilateral calculi should be investigated for the presence of hyperparathyreoidism, for this is the commonest presenting symptom of this rare disease. Priestley at the Mayo Clinic has produced evidence to show that in young adults with large branched calculi, nephrolithotomy gives a better expectation of life than a nephrectomy, even though extensive splitting of the kidney may have to be carried out.

Most surgeons use X-ray control at the operation table to ensure the removal of all stones. At the Mayo Clinic a handy aluminium holder is employed to steady the kidney while it is "screened" and films are taken.

Suby's solutions for dissolving stones have a rather restricted use and in most clinics are employed only in such cases as when small fragments have been left behind in a kidney after nephrolithotomy or in cases of encrusted cystitis. The dissolving of a renal calculus *in situ* is a prolonged, uncertain and uncomfortable business, though calculi have undoubtedly been removed in this way.

As for the controversial subject of dietary prevention of calculi, Higgins still gives vitamin *A* and employs a series of careful dietary régimes. Most urologists, however, are rather doubtful of the value of these measures. Jewett thinks that in the cases of uratic calculi or the rare cystine stones the urine should be kept alkaline. In the case of phosphatic calculi, while acidification of the urine does increase the solubility for phosphates, this effect may be nullified by increased excretion of calcium which occurs with an acid diet. Jewett believes that this latter effect is largely an individual peculiarity, and he considers that before a patient is subjected to the discomforts of an acid ash diet the effect of such a diet on his urinary excretion of calcium should be determined. All urologists agree that a large fluid intake is desirable for patients with calculi, that food with a high calcium content like milk and cheese should be avoided, and that such patients should not take vitamin *D*.

Prostatic Obstruction.

Indications for Operation.

The indication for operation for prostatic obstruction is obstruction at the vesical outlet and not the presence of an enlarged prostate. The size of the gland bears little relation to the degree of obstruction, and the amount of residual urine is but a poor guide, for a man with quite a severe grade of obstruction may have a well compensated bladder with hypertrophied muscle which enables it to empty well in spite of the difficulty. Symptoms of bladder-neck obstruction may be obvious enough, but occasionally the general malaise, loss of appetite and sleepiness of early uræmia may be the leading symptom, and symptoms of prostatism may be elicited only by careful questioning. In such cases operation is clearly indicated, but there is often difficulty in deciding the necessity for operation in milder cases. There is no harm in waiting six months and reviewing the position then, provided the patient is not suffering renal damage from back pressure. In such doubtful cases, however, an excretion pyelogram may be of great assistance. The presence or absence of hydronephrosis will show whether there has been serious back pressure on the kidneys, quite a good cystogram is obtained, which may show the amount of intravesical prostatic enlargement, and a film taken after micturition shows the amount of residual urine, without the patient's being subjected to the risks of instrumentation.

It is not generally realized that it is very difficult to form a correct estimate of the size of a prostate by rectal palpation alone. The only way a reasonably accurate estimate of size can be made is by rectal palpation with a urethral sound or a cystoscope in position, and the intravesical enlargement can be determined only by cystoscopy or by a cystogram. However, the main reason for wanting to know the size of the gland is to select the type of operation rather than to determine the necessity for it.

Pre-Operative Care.

There has been a general fall in mortality from prostatic surgery in recent years. There can be little doubt that this is mainly due to the use of the sulphonamides and antibiotics and the widespread use of blood transfusion. The protection afforded by these measures against the results of infection and hæmorrhage have allowed improvements in technique.

Few patients are now refused surgery. There is less need to sort out the poorer "risks", and consequently specific tests of renal function before operation are not now very widely used. In most clinics it is considered that the blood urea level is the most useful and a quite adequate index of the state of renal function. The patient, of course, is given a full medical examination, the urine is examined microscopically, and, if necessary, culturally, and a hæmoglobin estimation is done. This may be regarded as the minimal necessary pre-operative check-up, and in various clinics other investigations are carried out as well.

In an endeavour to preserve asepsis in a patient with clean urine, many urologists avoid as far as possible the passage of a catheter or any urethral instrument whatever before operation. This is quite feasible in most cases. Millin, for instance, usually makes a cystoscopic examination of his patients on the table immediately before proceeding with the operation. The first step in an endoscopic resection is an examination of the bladder, and where possible this is the first instrumentation. Wilson Hey, of Manchester, has carried this principle to its extreme limit and prefers to operate on a patient with acute retention of urine rather than pass a catheter. If emergency operation is not feasible he advises draining the bladder by the suprapubic route with a lumbar puncture needle and then operating within forty-eight hours. Even at operation he passes the urethral tube by the retrograde method. Whether the carrying of a good principle to these extreme limits to the exclusion of all other considerations is justified seems a bit doubtful, but he has done a service in stressing the importance of avoiding unnecessary instrumentation before operation.

If the urine is heavily infected or renal function grossly impaired, a period of catheter drainage may be required before operation. The Foley bag catheter in the United States has largely replaced other types as an inlying catheter. A small size (about 16 F) is usually employed, as it causes less urethral irritation.

Suprapubic Cystotomy.

Preliminary suprapubic drainage of the bladder is much less commonly carried out than formerly. Nesbit, Berry and others avoid it almost altogether, on the grounds that the mortality from this operation is as high as or higher than that of resection. This, it seems, is certainly true

when an open operation is performed. Riches in England and Higgins and Engel in the United States avoid many of the risks of this operation by blind suprapubic puncture of the distended bladder and the insertion of a small catheter about 16 F in size. Riches has designed an ingenious instrument which holds the catheter and carries it in behind a knife blade, but the method used by Higgins seems even better. He punctures the bladder with a small trocar and cannula. The trocar is removed, and a cystoscope telescope bearing a light is inserted. Thus the bladder can be inspected and the amount of intravesical enlargement of the prostate determined. The telescope is now removed, a catheter inserted and the cannula withdrawn over it.

Cystotomy, however, is an undesirable procedure and should be reserved for the worst "risks" with impaired renal function, in whom improvement may be expected following a long period of drainage.

Types of Prostatic Obstruction.

As you know there are three main types of prostatic disease which may cause vesical neck obstruction; they are benign hypertrophy or adenoma of the prostate, median bar or fibrous atrophy of the prostate, and carcinoma.

Benign hypertrophy or adenoma affects that portion of the gland adjacent to the urethra. It is apparently caused by some hormone imbalance, but once established it does not respond in any adequate degree to hormone therapy and must be dealt with by operative measures.

Median bar, fibrous atrophy of the prostate, or sclerosis of the bladder neck, as it is variously called, tends to cause trouble at an earlier age than adenoma, and the condition is thought to be due in part at least to chronic inflammation. The obstruction must again be dealt with by operation, but in many cases results are not as satisfactory as in the case of benign hypertrophy, as the condition is a fibrosis and may contract down after excision is performed, so that further operation or dilatation becomes necessary.

Carcinoma of the prostate occurs nearly always in the posterior lobe, which Huggins has shown to be a physiologically distinct portion of the gland. This portion of the prostate is not involved in the changes of benign hypertrophy, and it is this portion compressed by the adenoma which forms, at least in part, the false capsule from which the prostate is enucleated at operation.

Mode of Healing of Prostatic Bed.

The mode of healing of the prostatic bed after operation is of considerable interest. The prostate is removed from within a false capsule of compressed prostatic tissue and the raw surface of the prostatic bed has opening on to it ducts of innumerable glands. From these ducts a new epithelium spreads out rapidly over the raw surface.[a] Healing is thus comparable to healing of the skin after a Thiersch graft has been cut from it, or, in the case of resection, after a superficial burn. The removal of a prostate is thus not comparable to the removal of any other tumour, except, perhaps, the shaving off of a rhinophyma by the plastic surgeon. The suture of a gland-bearing surface like the prostatic bed, as is done in the Harris operation, is thus not really a logical procedure, and such sutures do not maintain permanent approximation of the surfaces except occasionally at the bladder neck where actual muscle is exposed. The bladder neck is always the last part to heal, for this is the only raw surface really devoid of epithelium and it is covered by epithelium creeping over it from the bladder mucosa or the prostatic bed.

Method of Dealing with Prostatic Obstruction.

There are many methods of dealing with prostatic obstruction and I propose to discuss briefly some of these methods now.

Transurethral Resection of the Prostate.

In the operation of transurethral resection of the prostate an instrument called a resectoscope is passed along the urethra and the gland is removed in small slices by a wire loop to which a diathermy cutting current is applied. Vision is obtained through a telescope with a lamp at the end, and the field is kept clear by a stream of water running through the instrument. Fragments of tissue are evacuated through the sheath of the instrument. Another variety of instrument uses a knife edge and the gland is punched away in small pieces.

Most urologists use this procedure for the median bar type of obstruction and for relieving obstruction due to carcinoma of the prostate. In these cases the gland cannot be enucleated, for there is no plane of cleavage, and there is little question that endoscopic resection is the best treatment for both these types of obstruction. However, in the case of benign hypertrophy there is wide variation in practice. From what I have seen of the operation and the post-operative course of patients after this and other procedures, it has seemed to me that endoscopic resection is the best operation for all glands which are within the limit of size which the individual surgeon can remove adequately within an hour's operating time, and the indications for the operation depend more on the skill of the resectionist than on the pathological condition present. In some clinics, for example at Ann Arbor, the Mayo Clinic and Kingston General Hospital, practically all prostates are dealt with by resection.

The operation has several advantages. The greatest is probably the absence of an abdominal incision, and the consequent absence of post-operative pain means that the patient can cough and move about freely in bed as soon as the spinal anæsthetic wears off; this is a most important consideration in the management of old people. No one with an abdominal incision will cough and move about freely in bed for the first twenty-four hours at least, whoever makes the incision.

Another advantage in dealing with patients in poor condition is that the operation can be stopped at any time, and it is probably the only operation which is actually easier at a second session than at the first.

The aim of the operation should be as complete a prostatectomy as can be carried out by open surgery. Many resectionists are undoubtedly able to perform an even more complete operation, removing the gland down to the true capsule. If a hole is merely tunnelled through or the resection is incomplete, the results are not satisfactory. Either the obstruction recurs or, if the remaining tissue is deprived of its blood supply, as commonly happens, then persistent pyuria may result from sloughing tissue in the prostatic fossa.

One interesting complication of the operation has been the occurrence of hæmoglobinæmia. This is not uncommon and hæmoglobin values may rise to 500 milligrammes *per centum* or more. Cases of anuria have occurred. The trouble is due to the use of water as the irrigating fluid. Blood from the cut prostatic surface is hæmolysed by the water and injected into the circulation through open vessels in the raw bed. This can be prevented by the use of an isotonic solution instead of water. Saline or any solution of an electrolyte cannot, however, be used, as in such a solution the cutting current will not work. Creevy uses 4% glucose solution, which is satisfactory except that it is a bit sticky; Nesbit uses a 1·1% solution of glycine, which seems to fulfil most requirements; and in Baltimore a 10% solution of mannitol is used.

A difficulty with the operation has been the size of the instrument. All urethræ are not constructed to accommodate a size 28 sheath, and the passage of too large an instrument is liable to result in a urethral stricture, an unfortunate complication of an operation designed to relieve urinary obstruction. Recently, Nesbit, working with the American Cystoscope Makers Incorporated, has produced an instrument with three sizes of sheath interchangeable on the one working element, and this seems to be a satisfactory answer to this difficulty. The instrument has only just come on the market.

There have been a number of other improvements in the instrument and technique. One is the use of a cutting current generated by electronic valves instead of a spark

gap. The current produced cuts much more easily and with minimal coagulation of tissue.

The mortality from this operation in good clinics is now very low. Nesbit recently reported 2000 cases with an overall mortality of 1·3%,[5] and the Mayo Clinic has a mortality of 1·2% (quoted by Gershom Thompson at a meeting of the American Urological Association in 1948). This is approaching an irreducible minimum, for it is to be remembered that the normal death rate of persons in the seventy-year age group approaches 1% per month. The only series of open operations that I know of which compare with these figures are Millin's personal series, in which the mortality rate is below 2% (quoted by Terence Millin at a meeting of the American Urological Association in 1948); but Nesbit's cases include the work of his resident medical officers learning the operation.

Retropubic Prostatectomy.

I have watched Millin carry out retropubic prostatectomy fifteen times, and in his hands it is undoubtedly a highly satisfactory operative procedure. It is accompanied by less post-operative bleeding and a smoother convalescence than follows the suprapubic operation. However, though Millin makes it look simple enough, in many cases it is not an easy operative procedure, and even in Millin's hands I have seen quite rapid hæmorrhage in the occasional case. In such circumstances Millin removes the gland quickly and then controls the bleeding. In no case did I see him lose more than six or eight ounces of blood, but in the hands of a less deft and assured operator the blood loss in some cases could have been considerable. The great advantage of the operation is that it allows a view of the prostatic bed, so that hæmorrhage can be controlled under vision; primary closure can thus be undertaken, and this preserves asepsis. In addition, the urethra is cut across at the gland apex with scissors, so that risk of damage to the sphincter muscle is avoided and small residual adenomata and tags of tissue, which may be left behind in operations by the suprapubic route, are easily seen and removed.

Riches, of the Middlesex Hospital, makes a vertical incision in the prostatic bed instead of a transverse incision. This avoids some bleeding and is rather easier to sew up, but if this incision is used it is wise to put (as Riches does) a preliminary suture transversely near the gland apex to prevent the incision tearing down into the external sphincter. Millin himself uses this incision for small fibrous glands.

Ogier Ward uses an incision running vertically from bladder into prostatic capsule. This gives a completely unobstructed view of both bladder and prostatic bed. Whether it entails any increased risk of fistula remains to be seen, but this complication had not troubled him in the 60 cases in which he had used the incision when I saw him at work, and the approach is certainly easier than Millin's.

A rare complication of prostatectomy, which seems to be more common with the retropubic operation, has been the occurrence of *osteitis pubis*. Why this condition should occur is rather a mystery at present, but infection probably spreads via the veins, by the same route by which carcinoma of the prostate metastasizes. Hamm, of New York, has had eight cases (not all following Millin's operation). These have occurred in spite of antibiotics. In his latest case incubation of material from the bone gave a pure culture of *Bacillus pyocyaneus*.

You are all familiar with suprapubic prostatectomy, and the perineal operation is but rarely performed in this country, so I will not discuss these procedures further here.

Carcinoma of the Prostate.

Carcinoma of the prostate is one of the commonest of all cancers. It arises almost always in the posterior lobe of the gland.

If the condition is diagnosed sufficiently early there is some hope of cure by radical surgery, and some urologists feel that if there is suspicion of carcinoma the prostate should be exposed by the perineal route and a biopsy taken. Then either a simple or a radical perineal prostatectomy can be performed, according to the result of examination of the frozen section. Millin prefers radical operation by the retropubic route, and Higgins told me that he was inclined to agree with him. Hugh Jewett produced at the meeting of the genito-urinary surgeons this year a report of the results of radical operation at the Brady Urological Institute over the last forty-five years. Of 132 patients operated upon during the period 1904 to 1943, 39% survived five years; in 78 of these patients the disease was confined within the capsule; and of these, more than 50% survived five or more years. The trouble is that in only 10% of 1961 cases was the condition operable so that only some 4% of patients presenting themselves with carcinoma of the prostate could be given a five-year survival by surgery.

The problem of surgery is thus, as in other parts of the body, that of early diagnosis. Needle biopsy had been discarded in all the clinics which I visited except at the Memorial Hospital in New York, where the method was used chiefly to get confirmatory evidence of carcinoma for research purposes.

At the Mayo Clinic, McDonald was working on the Papanicolaou technique of diagnosis of carcinoma by the search of various secretions for the presence of malignant cells. He regarded the method as of considerable value in the case of carcinoma of the lung, and thought that it held promise in the case of carcinoma of the urinary tract and possibly carcinoma of the prostate. He had some nice specimens of malignant cells expressed by prostatic massage. The most dangerous aspect of this method of diagnosis is the risk of "false positive" reports. McDonald had found that cells desquamated from the renal tubules looked rather like malignant cells, and he preferred to make his diagnosis on clumps of cells or fragments of tissue and not on single cells.

Œstrogen Therapy.

In spite of all this work, however, the fact is that the vast majority of patients with carcinoma of the prostate can be offered no hope of surgical cure, and a great comfort to these patients has been the introduction by Charles Huggins of the œstrogen treatment of cancer of the prostate. In a few cases the disease appears to be controlled indefinitely. In one of Huggins's first cases the patient is still alive and well with no detectable sign of carcinoma. Huggins thinks that one milligramme of stilbœstrol per day is an adequate dose which produces the maximal effect. He actually uses a little more to be sure that the patient is absorbing this dose, but recently very large doses have been used by other urologists in cases in which a break-away from hormonal control has occurred; a dose of 100 milligrammes per day is commonly given and in some of these cases the patients appear to have shown improvement again. There is difference of opinion as to when the hormone treatment should be given. Huggins feels that it should be given at once, in the hope of permanently inhibiting or actually curing the carcinoma; but Nesbit prefers to hold his hand against the day when the patient begins to suffer symptoms from his disease.

When œstrogens are given there is a lag period before the growth of the neoplasm is inhibited. For patients suffering severe pain orchidectomy gives much more rapid relief, and this operation makes sure that the patient is getting his therapy. Some old men may be none too regular in the swallowing of tablets.

In New York at the Memorial Hospital a variety of other hormones were being tried. No definite conclusions had been drawn, but it seems that it may be worth trying luteinizing hormones in cases in which a break-away from œstrogen control has occurred; at least no harm can be done, and X-ray treatment of the pituitary may also be tried with some hope of alleviation of symptoms. (In animals hypophysectomy produces a much more rapid and complete atrophy of the prostate than does orchidectomy.)

CARCINOMA OF THE BLADDER.

The treatment of bladder carcinoma is still unsatisfactory. The pathologist can estimate the malignancy of a bladder tumour in a number of different ways. Broder's classification, based on the number of malignant cells in a section relative to the number of normal forms, is used widely in the United States. The type of cell present is of importance; squamous and adenocarcinomatous change indicates a worse prognosis than if the tumour is of pseudostratified epithelium only. Jewett and also McDonald, however, have shown that the most important factor in deciding the prognosis is the degree of penetration of the bladder wall. Tumours which lie superficial to or have just begun to invade the muscle carry a good prognosis, while tumours which invade the deeper muscle layers or the perivesical fat carry a bad prognosis. At the Mayo Clinic these latter cases had only a 5% five-year survival rate with all forms of treatment.

All this, while not unexpected, has a bearing on treatment. At the moment probably the most favoured method of treatment for a frank carcinoma is a total cystectomy, but many surgeons are becoming doubtful if this is really the best form of management for these cases. In those cases with deep penetration of the bladder wall the results are poor, and in more superficial cases good results can be obtained by less drastic procedures. The average mortality of cystectomy and ureteric transplant in the United States of America at the present time is about 10%. Of the patients at least half develop some degree of hydronephrosis and impairment of renal function. An improved technique of uretero-intestinal anastomosis is badly needed. Nesbit has employed a new method which holds some promise. He simply makes an inch-long incision in the ureter and carries out a single-layer direct anastomosis to a corresponding incision in the large bowel. About a dozen patients have undergone this operation in Ann Arbor and some fourteen at the hands of Aberhardt in Toronto, and these have almost uniformly done well with a striking absence of dilatation of the kidney pelvises. This is, like retropubic prostatectomy, a revival of an old procedure which failed in the past (it was, in fact, the first method of anastomosis tried), but now with antibiotics and improved technique it becomes feasible. It would seem that if any surgeon is faced with a technical problem the literature to consult is that before 1900, when the attempts of the old surgeons can be tried over again with a background of safeguards which they never knew.

There have been two different reactions to the results of cystectomy. In the Memorial Hospital in New York, at the instigation of Brunschwig, who believes that the way to treat cancer is ruthless block removal of the involved tissue, a far more radical operative procedure is being tried by Marshall and Whitmore. The iliac and pelvic glands, the bladder, peritoneum and rectum, and in the female the uterus, vagina and Fallopian tubes are removed in one block, the muscles and nerves of the pelvis being left bare. The ureters are anastomosed to the large bowel just proximal to a colostomy and the small intestine is turned back into the raw pelvis with no attempt at reperitonizing the bare muscle. Seven such operations had been performed when I was there, with two deaths, but one of these was that of a man of seventy years in very poor condition. In two cases an anal pull-through operation had been performed in an attempt to obtain a functioning anus. The operation, though mutilating, is at least logical and in conformity with other successful cancer surgery, and since the iliac vessels and obturator nerves are almost the only structures which have to be treated with respect, it is not technically difficult for such an extensive operation.

Other surgeons feel that the mutilation from a total cystectomy is not justified by the results and prefer local removal. After all, a partial cystectomy removes just the same depth of tissue as the removal of the whole bladder. A superficial growth can be removed with the resectoscope together with the greater part of the underlying bladder wall, and in addition some surgeons implant radon.

In summary, it seems that nearly all the good results of total cystectomy are in cases of superficial growths; once the growth has penetrated the bladder wall the five-year survival rate drops to around 5%. It would seem that with superficial growths good results could be obtained by the less radical procedures, while patients with the deeper growths may be given some hope by a radical block dissection such as that used by Brunschwig.

I think that not many would quarrel with this view were it possible to distinguish the deep from the superficial growth, but at present this cannot be done with any degree of certainty, though Jewett considers a reasonably accurate opinion can be given after careful bimanual palpation.

One interesting development is a report of four cases of bladder papilloma treated with podophyllin by Semple of Saint Paul's Hospital in London.[6] I have not seen the treatment used, but I understand that Dr. Burnell has tried it in some cases and I would be very interested to hear his comments. The treatment is, of course, of proven value in the case of genital warts.

HYPOSPADIAS.

Denis Browne, of the Hospital for Sick Children, Great Ormond Street, has evolved a new operation for the cure of hypospadias. His procedure is both simple and effective, and 40 patients have now been operated upon without a failure—surely an unprecedented series. The operation has not yet been published. The essential princip'es are, firstly, that any cutaneous communication between urethra and skin will always form a permanent fistula and, secondly, that the penis seems to be free from the tendency to form keloidal scars.

The first stage of correcting the bowing is carried out much as usual at the age of about eighteen months, and then at the age of about four years the second stage is performed. A flat strip of skin is left running from the perineal opening of the urethra to the glans and is buried deep to everted skin edges. Relaxation is obtained by a simple dorsal incision which is left open. A small triangular plastic on each side of the glans draws the new meatus up to a normal position. The bladder is drained by a perineal urethrostomy. The flat skin strip forms itself into a new urethra in about ten days or less.

This operation really does seem to be the answer to the problem of hypospadias.

IMPROVEMENTS IN SCRUB-UP TECHNIQUE.

Soap containing "G.11" or "Gamophen", a new, effective, non-irritant, persistent antiseptic, is now on the market in the United States. The use of the soap was first reported by Traub and others in *Surgery, Gynecology and Obstetrics* in 1944. The routine ten-minute scrub is replaced with a two-minute wash during which the fingernails are cleaned with an orange stick. The results are better than with a routine scrub, and the bacterial count within the gloves remains low during the operation. Moreover, if no other soap is used bacterial counts on the hands decrease over the next two days. The soap or a cream containing "G.11" is in routine use at Ann Arbor, where experiments have confirmed its efficacy. Another interesting development is a new starch glove powder, "Bio-sorp" dusting powder (Johnson and Johnson). It is becoming widely realized that talc is an irritant substance and may be responsible for the formation of granulomata and adhesions. This new powder is a specially prepared corn starch which has been treated in some way which enables it to resist autoclaving. Although it feels a little coarser it seems to be rather a better lubricant than talc with which to pull on a glove, and it is non-irritating and completely absorbed in the tissues. This or some similar powder obviously should cause talc to be taken right out of the operating theatre.

A non-splash tap nozzle is also available. I saw these in use at Cleveland, where they were highly satisfactory. A foamy stream of water is produced, which allows economy in the use of sterile water and does not splash at all. This is more than just an æsthetic consideration, because a wet apron means an unsterile operating gown.

NEW METHODS AND APPLIANCES.

Gauze tampons containing a thread opaque to X-rays have been devised. In California everything is the biggest

in the world, including the law suits, and consequently these tampons are especially popular there. They are available commercially in America and could well be adopted for routine use everywhere.

A Cunningham incontinence clamp is made of flexible metal, allowing an individual fitting. Apart from their obvious use they have also been used with some success by V. J. O'Conor for the treatment of nocturnal enuresis in young men. A clamp is applied before retiring and the pain of his distended urethra wakes the patient when he micturates during sleep. After a while a conditioned reflex becomes established, so that he wakes before he gets hurt, and then the clamp may be in time discarded.

A pair of artery forceps with bakelite-covered handles, as used by Dr. Riches, of the Middlesex Hospital in England, makes a most useful general purpose diathermy instrument. A diathermy knife is made by holding a needle in the jaws. When not in use it is clipped onto the operating drape and this overcomes the constant nuisance of having the diathermy instruments falling off the table.

Conclusion.

In conclusion I should like to add a word of gratitude for the generosity of the Carnegie Corporation for providing the travelling fellowship without which this trip would not have been possible.

I should like to express my appreciation of the honour done me in asking me to address the meeting and thank you for your attention.

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Reports of Cases.

SPIGELIAN HERNIA: REPORT OF A CASE.

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A Spigelian hernia is one which occurs through the semilunar line (Spigel's line), lateral to the rectus muscle.

The majority occur through the lower half of this line and most of the cases described have occurred at the level of the semicircular line of Douglas—the curved lower edge of the posterior layer of the rectus sheath.

Clinical Record.

L.W.McN., a male, aged sixty-three years, who was employed as a fitter in the railways, reported a slight aching pain in the lower part of the abdomen, on the left side, in February, 1948, following a small twisting movement of his body. He was seen soon after by two doctors, who confirmed the presence of a "hernia in the left groin".

He noticed the hernia himself and described it as "a small muscle protruding through the lower part of the abdomen on the left side".

On examination of the abdomen there was an ill-defined swelling in the left lower quadrant; it was painless, soft, and readily reducible and gave an impulse on coughing. It was thought to be a direct inguinal hernia.

The patient had suffered from dysuria and nocturnal frequency for several years, and on August 17, 1948, a transurethral resection of the prostate was carried out.

At operation on August 24, 1948, there was no sign of a direct inguinal hernia; exploration of the cord and internal inguinal ring revealed a small indirect hernial sac about one inch long and without any contents; this was removed in the usual manner. However, as this indirect inguinal hernia did not seem large enough to account for the swelling seen pre-operatively, a further search medially revealed a definite swelling occurring through the semilunar line, at the level of the semicircular line of Douglas. There was a deficiency about one inch in diameter in the aponeurosis of the *transversus abdominis* and internal oblique muscles at this level. This gap was repaired with a fascial flap taken from the anterior rectus sheath. The post-operative course was uneventful and the patient left hospital eighteen days after his operation.

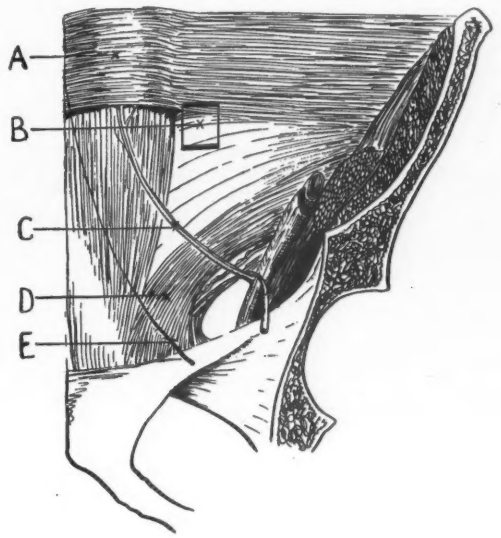

Figure I.

The anatomy of the Spigelian sheath. A. Posterior rectus sheath. B. Spigelian hernia. C. Deep epigastric vessels. D. Conjoined tendon. E. Obliterated hypogastric artery.

Comment.

A Spigelian hernia is a rare form of hernia. It was first described as occurring through Spigel's line by Klinkosch in 1864, though spontaneous lateral ventral hernia had been known to occur for some years previously.

Up to 1942, 120 cases had been reported in the literature, mostly in Continental journals. There were only eight cases reported in the American literature, and fewer still in the British journals. I could find no mention of it in the recognized English text-books of surgery.

The cause is generally stated to be a congenital deficiency in the semilunar line; cases have been described in young children. Occasionally a branch of the deep inferior epigastric artery has been described emerging through the hernial ring, and this was thought to be a possible ætiological factor; however, it has not been found in every case.

Some authorities have postulated the presence of a small congenital defect, slowly widened by the outward pull of an accessory slip of the internal oblique muscle, which has been found at this site in some people.

Also a pre-peritoneal lipoma, found overlying the hernia in some cases, has been put forward as a possible predisposing factor.

Finally, excessive straining has frequently been a feature in the history of patients with Spigelian hernia, and in very many of the cases reported additional types of hernia are present.

It is of interest that in the present case there was a long history of repeated straining at micturition, due to an enlarged prostate, and in addition there was a small indirect inguinal hernia present.

The hernia penetrates the deficiency in the aponeurosis of the transversus and internal oblique muscles, but usually does not penetrate the external oblique aponeurosis. Spreading out under this latter layer, it forms a type of "interparietal hernia" of the lower part of the abdomen.

In many cases the diameter of the neck is quite small (0·5 centimetre), and it is in such cases that strangulation is very prone to occur; for this reason operation should be advised as soon as possible.

Conclusions.

Attention has been drawn to the occurrence of Spigelian hernia for the following reasons.

1. It can be a cause of aching pain in the lower part of the abdomen easily overlooked.
2. It has been missed during operation for an inguinal hernia, and subsequently regarded as a recurrent direct inguinal hernia.
3. In many cases it is very liable to strangulation.

Acknowledgement.

I wish to thank Dr. F. J. Colahan, of Saint Vincent's Hospital, Melbourne, for permission to report this case; also Miss Andrew, librarian of the Royal Australasian College of Surgeons, who has been most helpful with the bibliography.

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UNUSUAL COMPLICATIONS OF FEMORAL HERNIA.

By W. M. DAVIES,
Colac, Victoria.

THE following case of femoral hernia is presented because of its rather unusual combination of complications.

Clinical Record.

The patient, Mrs. S.W., aged fifty-four years, was admitted to hospital on January 30, 1948. She complained that she had had a "rupture" for many years, which previously had given her no trouble. Six days prior to admission she had begun to feel nauseated and noticed that the hernia had become irreducible. She was not worried until the previous day, when the lump had become very painful and she vomited. Both these symptoms had become increasingly severe. There were no other complaints, the bowels having been open on the day of admission.

The pulse rate was 104 per minute and the temperature 99·4° F. Examination revealed no abnormality in the circulatory, respiratory or nervous systems, and the abdomen, apart from tenderness in the right iliac fossa, was normal. There was a tense, tender lump in the right inguinal region below Poupart's ligament and lateral to the pubic spine. This could not be reduced and there was no impulse on coughing. Pelvic examination revealed acute tenderness in the right fornix, but otherwise no abnormality.

A diagnosis of irreducible femoral hernia was made and operation under open ether anæsthesia was carried out. An oblique incision was made half an inch above Poupart's ligament and a sac one and a half inches in diameter was found presenting from the femoral canal. When the sac was opened turbid fluid escaped and a piece of dark gangrenous-looking bowel was seen. The inguinal canal was opened, the neck of the sac was incised, the contents were reduced, and the entire sac was pulled upward. The contents were found to consist of an acutely inflamed appendix, which was covered with fibrin and had two areas of gangrene, one of which corresponded to the constriction caused by the neck of the sac. Routine appendicectomy was performed. The posterior wall of the sac was formed by the caecum. This was drawn upward, the femoral canal closed in the usual manner, and the peritoneal opening sutured. External oblique muscle, Scarpa's fascia and skin were then closed.

The patient on return to the ward was given 30,000 units of penicillin four-hourly for four days and convalescence was uneventful.

Comment.

Although it is generally recognized that inguinal hernia may contain almost any abdominal viscus, it is uncommon to see acute appendicitis associated with sliding femoral hernia, and it is a point of interest in this case whether the irreducibility of the hernia was due to the inflammatory changes in the appendix, whether the inflammation followed strangulation, or whether the conditions were merely coincidental. It appears likely that the explanation is provided by the first of these possibilities.

Reviews.

A YEAR BOOK ON RADIOLOGY.

"THE 1948 Year Book of Radiology" has been received.[1] This edition marks the advent of new editors for the diagnostic section, Fred Jenner Hodges and John Floyd Holt of the University of Michigan, and they have certainly made a good job of the task. The therapeutic section is still in the capable hands of Ira I. Kaplan and Sidney Rubenfeld.

After a short section on technique, the various reviews of a voluminous current literature are dealt with in order, the head, spine, extremities, chest, gastro-intestinal tract and genito-urinary tract being included. The editors add small comments from time to time on the various articles. The illustrations are of excellent quality and are produced in the original "negative", which is of great value to the radiologist who always works with "negative" pictures.

The section on technique features the application of the Bernard Schmidt reflector camera to radiology. This novel camera (designed for use in astronomy) has been used for the production of miniature films. It shortens exposure by from four to six times. An ordinary 70 millimetre film exposure requires a skin dose of 1*r*, twenty times the exposure for an ordinary film. This shortening of exposure would thus diminish the risk of damaging the patient's skin.

In osteoporosis, Brabararitz (Geneva) states that 30% to 50% calcium loss is necessary before it can be demonstrated in an X-ray film. Apparently protein metabolism plays a considerable part in calcium loss. Most authors agree that clinical signs are of more importance than radiological signs in vertebral disk lesions. An interesting article discusses calcareous deposits in the region of the head of the humerus and femur. These conditions are considered to be due to disturbance of vessels and not to disturbed vitamin or calcium metabolism.

Pneumarthrography is still in favour for investigation of various conditions in the knee joint.

Brailsford complains about the unreliability of histological examination in the diagnosis of bone tumours, and still considers careful evaluation of the clinical and radiological

[1] "The 1948 Year Book of Radiology"; Diagnosis—edited by Fred Jenner Hodges, M.D., associate editor, John Floyd Holt, M.D.; Therapeutics—edited by Ira I. Kaplan, M.D., F.A.C.R., associate editor, Sidney Rubenfeld, M.D., F.A.C.R.; 1948. Chicago: The Year Book Publishers Incorporated. 9" × 6", pp. 476, with many illustrations. Price: $6.50.

evidence of the greatest importance. He points out that spectacular radiological evidence is liable to misinterpretation by inexperienced observers.

Cooper reports an interesting epidemic of lead poisoning in children due to the inhalation of fumes from burning old battery cases. The epidemic was discovered only after X-ray examination.

More interesting work is reported in the field of arteriography. A safer contrast drug than "Thorotrast" is still being sought.

Authors point out that many calcified areas found in the lung fields are due to *Histoplasma capsulatus* and not to tuberculosis. Beryllium workers have been found to develop a condition closely resembling silicosis after an exposure of only ten months. Vagotomy is discussed by various authors. Symptoms are relieved at once and the ulcer crater disappears. It is too early yet to evaluate this rather drastic operation. Cattell and Boehme report ten cases of malignant disease complicating chronic colitis. The change usually occurs in the recto-sigmoid area. Alyea and Haines report on the intradermal test before excretion pyelography—86% of patients gave no local reaction and of these 4% had a generalized reaction after injection; 14% gave a positive reaction and of these 16% had a generalized reaction on intravenous injection. Slow injection intravenously is called for and if no reaction occurs after the injection of 1·0 millilitre in three minutes the remaining solution may be given with safety.

The section on radiotherapy is introduced by a general discussion of various therapeutic procedures. No hormone, enzyme or chemical substances have proved satisfactory, although some offered relief in cancer. The use of radio-isotopes has in general proved disappointing. Radiation sickness has yielded in many cases to the administration of hydrochloric acid. A section on radiation biology is of interest. Little change is reported in methods of radiation.

This book should receive a place in every radiologist's library.

THE SEARCH FOR HEALTH.

A NEW addition to the series of booklets known as "The Thinker's Library" is "The Search for Health" by D. Stark Murray, and as stated on the cover it consists of "an outline in simple language of the causes and scientific treatment of disease". Naturally such a booklet is for laymen who wish to learn more about the causes of the various maladies to which the flesh is heir, and while for such readers the booklet will doubtless be of interest, it will really make them think and perhaps even confuse them on some of the topics discussed, for the problem in writing such works is as to just how much detail should be included or omitted. The author, however, has written interesting chapters on such subjects as the germ theory of disease, parasites, healthy minds and healthy bodies, to mention only three, as well as a peroration upon the future, and he has certainly provided the thinkers among his readers with plenty of food for thought.

"BIOLOGICAL BRICKS AND MORTAR."

SOME years ago we reviewed an unusual book with the popular title "The Stuff We're Made Of", written by W. O. Kermack and P. Eggleton, both highly qualified scientists from Edinburgh; and now, after two reprintings, a second edition has come to hand.[2] Looking back a whole decade, which may be regarded as a remote period in the modern scientific sense, we find that we then expressed some wonder and surprise at the remarkable developments that were taking place in the biochemist's laboratory; so many of Nature's closest secrets were being revealed in rapid succession. However, much oxide of hydrogen has passed under the biochemical bridge in those intervening years, and now we find ourselves contemplating the latest developments with a calm and collected complacency.

In the new edition of this delightful book, which is written in a fluent, scholarly and entertaining style, there are a few obvious changes, such as a minor rearrangement of the illustrations and the inclusion of a great deal of fresh material in the text to show the significance of recent physical and chemical research in biological processes. With all this new knowledge it gives a decided uplift to one's professional self-respect to feel a little more conversant with the peculiar constitution and behaviour of atoms, colloids, protons and electrons; or to improve one's sense of proportion by a clearer conception of the relative dimensions of a protein molecule as compared with those of the full moon.

The keen student of medicine will discover in the pages of this volume a great deal of useful knowledge with a practical application in his professional work; he will become more familiar with the complex organic and inorganic substances which enter into the make-up of everything belonging to the animal and vegetable kingdoms, and will soon find himself on intimate terms with the enzymes, vitamins, hormones, bacteria and viruses, which have a way of intruding themselves upon the medical practitioner's attention in a variety of situations. Most of us have only a dim recollection of those heart-rending encounters with the fundamental sciences as we set out upon a medical career; but these pages are full of salutary reminders of the fact that the greatly extended powers of healing that we possess today are largely due to new developments in this fertile field of investigation.

PRACTICAL ENDOCRINOLOGY.

THE preface to "The Practice of Endocrinology", edited by Raymond Greene, indicates that it is written in the main for the general practitioner.

Professor Dodds of the Middlesex Hospital once said that no subject had been so abused as hormone therapy with the exception of thyreoid and adrenaline, both of which were introduced at the end of the last century. His additional remarks concerning the appalling quackery practised from the sweepings of the abattoir floors and the inundation of the doctor's desk by manufacturing firms with what is euphemistically called "literature" have a measure of truth in them. Bearing these thoughts in mind, we feel that the author has accomplished what he has set out to do—to give the busy general practitioner, and practising physician for that matter, a useful practical manual. It is stripped of much theorizing and academic detail. Throughout, a sensible balance is kept between known facts and practical application, especially in relation to tried therapy. Where there is doubt as to efficacy this has been clearly indicated.

The illustrations are well produced and this facilitates recognition of various clinical states. The book is readable and it is well set up and annotated.

Chapter VII on diabetes is well extracted and one perceives the hand of one of the associated authors and his well-known text-book. For those seeking a purely practical book on this subject with much of the verbiage of the completer works removed it can be well recommended. Greene (with his six first-class physician collaborators) has produced a useful book from the practitioner's point of view.

PRACTICAL BIOCHEMISTRY.

THE principal changes in the fifth edition of Koch and Hanke's "Practical Methods in Biochemistry"[2] are the introduction of a chapter on the use of microbiological methods for the detection of certain vitamins of the *B* group and of certain amino acids, and some extension of the description of Van Slyke manometric methods of analysis.

The book is intended for medical students, but the matter presented is strictly limited to descriptions of laboratory tests and estimations. This is very useful for the laboratory worker, but such a limitation is undesirable from the point of view of the medical student. The methods of obtaining specimens for analysis and the interpretation of results are often more important to him than actual laboratory procedures.

While the range of tests and estimations described is in some ways wider than usual, there are serious gaps. In the section on cellular constituents, for example, there

[1] "The Search for Health", by D. Stark Murray, B.Sc., M.B., Ch.B.; 1948. London: Watts and Company, Limited. 6¼" × 4", pp. 172, with 19 illustrations. Price: 2s. 6d.

[2] "The Stuff We're Made Of", by W. O. Kermack, M.A., D.Sc., LL.D., F.R.S., and P. Eggleton, D.Sc., F.R.S.E.; Second Edition; 1948. London: Edward Arnold and Company. 7¾" × 4¾", pp. 368, with illustrations. Price: 10s. 6d.

[1] "The Practice of Endocrinology, edited by Raymond Greene, M.A., D.M., M.R.C.P.; 1948. London: Eyre and Spottiswoode (Publishers), Limited. 9½" × 6", pp. 392, with illustrations, some of them coloured. Price: 52s. 6d.

[2] "Practical Methods in Biochemistry", by Frederick C. Koch and Martin E. Hanke; Fifth Edition; 1948. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5", pp. 430. Price: 22s. 6d.

is no mention of inorganic constituents. In Part II on the chemistry of the digestive tract the fæces are not even mentioned, nor is there any mention of the fractional test meal. In Section III on blood and urine a similar omission of all functional tests occurs. An extremely short chapter occurs on chemical tests for hormones. This is limited almost entirely to qualitative tests. The now commonly used quantitative application of Zimmermann's colour reaction to the estimation of 17-ketosteroids is not considered.

This laboratory manual originated as the practical section of Matthews's text-book of physiological chemistry. It gives the impression that it has never been satisfactorily adapted to the changed requirements resulting from its removal from the parent volume.

The book is well produced. Its comprehensive index and appendix on the reagents used add to its value in the biochemical laboratory.

A MEDICAL HANDBOOK.

THE fifth edition of the "Physician's Handbook",[1] by John Warkentin and Jack D. Lange, merits the same praise that we gave to the fourth edition. A good deal of the material in this pocket reference book remains unaltered, but certain changes have been made to bring the information up to date notably in relation to hormones, and additions have been made to the already wide range of subjects; a section on the diagnosis and treatment of acute poisoning fills one of the few gaps in the previous edition. The reference value of the book has been enhanced by the printing on the inside back and front covers of tables showing the normal findings in blood and cerebro-spinal fluid examination (including chemical analysis) and in liver and renal function tests. On the outside back cover is a table of approximate equivalents (apothecary and metric) of weights and volumes, as well as milliequivalent conversion factors. The book is of handy size with no waste space, and the practising doctor who slips it into his pocket or bag should find it a great aid.

HYGIENE IN INDUSTRY.

ELEVEN different writers, each a specialist in his own particular field, have contributed the fifteen chapters which comprise Volume I of "Industrial Hygiene and Toxicology", the latest American book on this subject, which was edited by Frank A. Patty.[2] The contributors are representative both of private industry and of government agencies. The editor, who has also written five of the chapters, defines industrial hygiene as "the science and art of preserving health through the recognition, evaluation, and control of environmental causes and sources of illness in industry". A study of the contents reveals the comprehensive scope of industrial hygiene, and the fact that only three of the contributors are medical men illustrates that not only the physician, but also the chemist, physicist, engineer and other professional groups, have important specialist parts to play in promoting the health, safety and welfare of workers in industry.

The editor states: "The object of this book is to present industrial hygiene and toxicology in simple, understandable terms in sufficient detail to be of some use to all persons interested in safeguarding the health and welfare of working people and in improving the working environment." This aim has been successfully achieved.

The first three chapters are concerned with the historical background and future role of industrial hygiene, records and reports, and the procedure for conducting an industrial hygiene survey.

The subject of fatigue and competence is discussed from two aspects—the personal and the environmental factors involved. Psychological influences have not been ignored, for it is pointed out that: "Mental efficiency is now much more important to industry than muscular efficiency . . .", and: "Wartime experience proved that some of the most 'ideal' combinations of temperature, humidity and air motion resulted in widespread complaints of monotony, indicating the complex psychological aspects of air conditioning."

The physiological effects of abnormal atmospheric pressure are discussed in satisfactory detail and then in sequence come chapters on: the mode of entry and action of toxic materials; sampling and analysis of atmospheric contaminants; radiant energy and radium; ventilation; occupational dermatoses; the visible marks of occupation and occupational diseases; fire and explosion hazards of combustible gases and vapours and of combustible dusts; respirators and respiratory protective devices; and lastly, dust and its role in the causation of occupational disease.

Space does not permit detailed comment chapter by chapter, nor is such comment necessary. One may, however, refer briefly to the "medical" chapters. That on occupational dermatoses was written by Louis Schwartz, the best known contemporary authority on this subject.

An offering by Carey McCord contains, in tabular form, useful information about common external marks or signs of occupation and occupational diseases and their cause and significance.

The contribution on dust in relation to occupational disease is based largely upon the work of several recognized authorities, and is chiefly concerned with pulmonary conditions. Attention is drawn to animal experimental work by other investigators, which showed that silica particles less than 0·6 micron in diameter caused much more liver fibrosis than larger particles. In the interesting section on the evaluation of disability in silicosis, various tests for ventilatory efficiency and for respiratory insufficiency are discussed.

In respect of exercise tests in general, the author favours the Master two-step test and states that it has definite advantages as it has been well standardized at least for cardiac function as to age and sex, is simple to perform, and is almost quantitative in terms of foot-pounds of work per given time. Although an appropriate reference to the literature concerning this test is given, further details in the text would be desirable. One cannot but agree with the following remarks: "From an economic and sociological point of view, it may be wrong to consider a patient as having disability if experience demonstrates that he is capable of doing his daily work. This is especially true if conditions are such that aggravation of an existing condition is unlikely."

This book is a notable addition to the literature on industrial hygiene. There is relatively little in it that is new, but mainly because of the wise choice of subject matter and the sound manner in which it has been arranged and presented, the book creates a most favourable impression. Here within a single volume is a wealth of information, in the search for which, until now, it has been necessary to turn to a number of separate publications. Any criticisms which one could make are only minor and, in view of the general high standard of this volume, there is little point in detailing them. This is a first-class reference manual, particularly suitable not only for the specialist in industrial hygiene, whether he is medically trained or otherwise, but also for the teaching and training of newcomers into this ever-expanding and absorbing branch of public health.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Psychological Medicine: A Short Introduction to Psychiatry with an Appendix on Psychiatry Associated with War Conditions", by Desmond Curran, M.B., F.R.C.P., D.P.M., and the late Eric Guttmann, M.D., M.R.C.P., with a foreword by Sir John J. Conybeare, M.C., D.M. (Oxon), F.R.C.P. Third Edition; 1949. Edinburgh: E. and S. Livingstone, Limited. 8¼" × 5¼", pp. 264, with 20 illustrations. Price: 12s. 6d.

For the general practitioner that he may "familiarize himself with the more practical aspects of psychiatry".

"Your Hospital Heritage and Future", by A. R. J. Wise, with a foreword by Sir E. Rock Carling, F.R.C.S., F.R.C.P., F.F.R.; 1949. London: William Heinemann (Medical Books), Limited. 8¼" × 5¼", pp. 270, with 50 illustrations. Price: 15s.

A book on the problems of the modern hospital, intended for persons associated with hospitals—voluntary workers and members of the medical, nursing, administrative and nursing staffs.

"Sex and Marriage", by Norman Robertson; 1949. London: Research Books, Limited. 7¾" × 5", pp. 56. Price: 2s. 6d.

Intended as a guide to sex conduct for men and women.

[1] "Physician's Handbook", by John Warkentin, Ph.D., M.D., and Jack D. Lange, M.S., M.D.; Fifth Edition; 1948. California: Univeristy Medical Publishers. 6¼" × 4", pp. 300, with illustrations. Price: $2.00.

[2] "Industrial Hygiene and Toxicology", edited by Frank A. Patty; Volume I; 1948. New York: Interscience Publishers, Incorporated. 10" × 6¼", pp. 564, with few illustrations. Price: $10.00.

The Medical Journal of Australia

SATURDAY, MAY 7, 1949.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A MATERNITY SURVEY IN BRITAIN.

THE time has long passed when it was looked upon as fit and proper to consider man as being able to divide his life and even his daily existence into so many isolated phases. Either a man was at work, or he was at play; either he was at war or he was at peace; either he was well or he was ill. Most people today know that man is not a creature of the moment. What a man does today will have an effect on what he will do tomorrow; how a man lives today will influence his outlook on life tomorrow; his state of health today, whether he is well or ill, will have a bearing on his general attitude to life tomorrow. Those whose lives are occupied by the study of man in health and disease know that what are spoken of as preventive medicine, curative medicine and social medicine are part of one entity and that no hard and fast dividing line can be drawn between any two of them. In such common events as pregnancy and childbirth the health of the mother and of all the other members of the home is of primary importance; but no one will deny that if the ultimate good of the mother, of her child and of the community is to be brought into the picture, social circumstances and economic status should not be forgotten. To neglect these considerations is to impose an undue burden on the mother and a heavy handicap on the child. The Commonwealth Parliament had very good reason in 1912 for the framing and passing of the *Maternity Allowance Act*, according to which a cash benefit was paid in respect of each confinement resulting in the birth of a viable child whether such child was born alive or dead. If an intelligent approach to this subject is to be made, it must be made on facts. A survey made recently in Great Britain has supplied some useful facts.[1]

The Joint Committee which undertook this survey was formed by the Population Investigation Committee and the Royal College of Obstetricians and Gynæcologists. The chairman of the Committee was James Young, M.D., F.R.C.S., F.R.C.O.G.; the actual direction of the inquiry was in the hands of Dr. J. W. B. Douglas and he was assisted by Miss G. Rowntree who was research assistant. The costs of the inquiry were met by a grant from the Nuffield Foundation and a donation from the National Birthday Trust Fund. The Committee held that effective policies for removing the deterrents to parenthood and for increasing the availability and efficiency of the maternity services could be framed only on the basis of a study of the problems actually encountered by mothers of the present day. The following were the main questions requiring investigation: (*a*) The availability of the maternity services to different social classes, and in different parts of the country. (*b*) The use made of these services. (*c*) Their effectiveness in educating mothers, and in reducing mortality and morbidity among mothers and infants. (*d*) The need for domestic help during pregnancy and the puerperium. (*e*) The nature and extent of present-day expenditure on childbirth. It was decided to take as the sample of mothers to be interviewed, all women who were delivered in England, Wales and Scotland during a single week. The week chosen was March 3 to 9, 1946, and the time of the interview was to be at least eight weeks after the birth of the baby. The inquiry was made by means of *questionnaires*, which were filled in by mothers in the presence of a health visitor. The magnitude of the undertaking is shown by the fact that 424 (92%) of 458 local authorities in England, Wales and Scotland agreed to allow their health visitors to undertake the interviews. A total of 13,687 mothers cooperated and of these 7287 answered questions dealing mainly with the availability of maternity services and the use made of them; 6400 answered questions on medical and other costs associated with the birth of their babies. Less than 2% of mothers refused to give interviews; a further 7% could not be interviewed because they were away or ill.

In regard to antenatal supervision, it was found that municipal antenatal services were used by all sections of the community; one-third of the mothers in the most prosperous group used them. In all 72% of mothers were supervised by local authority schemes. It was found that in spite of the incentives for mothers to come under supervision early in pregnancy, many did not do so until the last three months, when it was too late for them to gain the full benefit of supervision. Domestic ties and the difficulty of leaving young children were reasons for late attendance in many instances, but even in the most prosperous groups supervision was sought much later than was thought to be desirable. To obtain the full benefit of supervision routine attendances should start in the first three months, but even in the most favourable conditions even less than half the expectant mothers attended as early as this. An interesting point is made in regard to examination by a medical practitioner at every visit of an expectant mother to a clinic. It is suggested that if a consultation with a doctor takes place at every visit there is a possibility that the abnormal side of the pregnancy will be emphasized. Practitioners in this country, who are accustomed to seeing their patients regularly throughout the whole of their pregnancies, will not agree with this. The impression left on the patient will of course depend on the way in which the practitioner handles the situation.

[1] Maternity in Great Britain: A Survey of Social and Economic Aspects of Pregnancy and Childbirth Undertaken by a Joint Committee of the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee; 1948. London: Geoffrey Cumberlege, Oxford University Press. 8¼" × 5½", pp. 278. Price: 12s. 6d. net.

It has to be remembered that a medical examination by a practitioner must not be hurried or perfunctory. A description is given of one clinic at which a doctor saw 29 patients in 80 minutes. A health visitor, it is true, had seen each woman and taken her history, but examinations made at this rate cannot be expected to create a bond of sympathy or confidence between patient and doctor, even if the doctor could be certain that he had made himself acquainted with the patient's physical condition, which is doubtful. One cannot but agree with the suggestion that in these circumstances it would be better for routine supervision to be made by a midwife or health visitor and for the doctor to concentrate his attention on first attendances, suspected abnormalities and the later stages of pregnancy. In private practice in this country many practitioners find it convenient to allot certain afternoons to antenatal supervision and expectant mothers attend regularly by appointment. There is no reason why appointments should not be made for patients at hospital clinics.

The place of confinement was investigated. Great variations were found in different areas. It is interesting to note that private beds in nursing homes and hospitals (a "nursing home" in Britain is the equivalent of a private hospital in Australia) supplied nearly one quarter of all institutional beds. During 1946 the percentage of institutional confinements was 54; in hospitals the percentage was 41 and in private beds 13. An interesting table is given of the circumstances of confinement for each occupational group. In 1944 the Royal College of Obstetricians and Gynæcologists recommended that all *primigravidæ*, all patients with abnormalities and all women with unsuitable home conditions should be confined in institutions. Since all types of beds in institutions are not equally available in all parts of the country, it is not really fair to try to discover how far this aim has been achieved. The members of the professional and salaried groups are comparatively free to choose their place of confinement; their habits therefore are likely to give a clue to the way in which the demand for maternity beds may change as housing conditions improve and the present shortages of beds and domestic help are remedied. Three-quarters of the confinements of wives of professional and salaried workers took place in institutions. They used private beds in nursing homes nearly twice as frequently as they used beds in public wards. However, the greatest numerical demand for such beds was made by wives of manual workers who occupied 39% of nursing home and private ward beds; the percentage of these beds occupied by wives of professional and salaried workers was only 31. One of the recommendations of the Royal College was not fulfilled by the wives of the professional and salaried workers—that no *primigravida* should be delivered at home. More than three-quarters of the 15% of *primigravidæ* who had their confinement at home, did so from choice; only one-sixth because they could not find accommodation elsewhere. Consideration of the mothers' second and third confinements from the point of view of hospitalization shows that it is only among the professional and salaried workers that an increase in size of family does not result in substantial economies at the birth of subsequent children. The question of domestic ties in relation to place of confinement is discussed, but can merely be mentioned here. The general indication from the survey is stated that a large proportion of mothers would prefer a good domiciliary maternity service, provided that some domestic help was available and housing conditions were improved. On the other hand, if sufficient maternity beds are provided in suitable institutions and if provision is made for the care of older children during the lying-in period, "there is little doubt that in England, as in America, the institutional habit would be established for the large majority of confinements". This conclusion will probably hold for Australia.

In regard to the cost of childbearing it is pointed out that the inquiry was made at a time when price control and rationing had probably reduced social group differences in expenditure. For all this, large differences were found. The most prosperous spent nearly twice as much as the poorest groups on first confinements—£57 and £31 respectively. A good deal of this money was spent on non-medical equipment such as the layette and the perambulator. The average working family spends about £28 on childbirth and receives only £6 in maternity grants. The opinion is expressed that a policy to reduce childbirth costs substantially would be successful only if it assisted mothers with their non-medical expenditure. This could be done, it is suggested, either by the provision of increased maternity grants or by reductions in the retail prices of certain goods. The Swedish measures are mentioned and justly. In that country families with low incomes who find the ordinary maternity grant insufficient to cover the essential costs, can apply to a special fund for additional aid for specified items, including clothing, equipment, dental care, additional food and domestic help; assistance up to 400 Kronen (about £27) can be given. "The successful operation of this scheme in Sweden shows how much more could be done in Britain and elsewhere to relieve families of the heavy outlay associated with childbirth."

There are other aspects of this inquiry that have not been mentioned. Clearly the whole matter cannot be covered in this place. Two conclusions perhaps may be stated. One is that there is need for a periodical check or inquiry into the efficiency of the maternity services of a community. Especially is this necessary when the health services of the community are under review. The other is that any inquiry must not cease with the puerperium. The state of the mother after childbirth and that of the child after his entry into the world need to be covered.

Current Comment.

CHRONIC ULCERATIVE COLITIS.

PERHAPS the most arresting features of the discussion at the Perth Congress on ulcerative colitis were the revival of surgical drainage, the hope of substituting intubation drainage as an emergency or temporary measure, and the use of intravenous alimentation for the double purpose of securing rest and ensuring absorption of food. The seriousness of this unsolved disease is only matched by the unhappiness of the physical and mental lot of the victims. T. Grier Miller and Thomas E. Machella have written a brief article which sums up the position.[1] They begin by remarking that the treatment of chronic ulcerative colitis is as poorly defined as its ætiology.

[1] *The American Journal of the Medical Sciences*, October, 1948.

Surgical intervention is much in the position that it occupied twenty years ago, but Coates and Dunlop, with a unique experience in the Japanese prison camps, have shown it should be the subject of serious thought again. Miller and Machella state that ileostomy would be an ideal therapeutic procedure if it were not for the drawbacks of the stoma which is usually permanent. Even the alteration of the patient's alimentary physiology, which gives him the greater comfort of a less fluid stool, is not great consolation, though an active and useful life may be followed in favourable circumstances. Whatever the decision about surgery in the individual instance, with regard to the lesser procedure of drainage or the major one of excision, it should not be deferred until strength and hope are exhausted. Machella claims that the non-mutilating procedure of "medical" ileostomy, or incubation, can give results comparable with external drainage. The difficulties of this method are considerable, as was shown in the Australian discussion, but they may not be insurmountable. Miller and Machella point out, too, that little is known as yet about the disturbances of function of the digestive system in this disease, particularly in absorption of the various components of a life-sustaining diet. They further think that the large amount aspirated in the first few days after intubation is established is significant, pointing out that the excessive quantity of material ejected from the ileum into the caecum is responsible for the increase in irritability and contractility of this organ. If this is so, it will be necessary to revise the pathological ideas still usually taught, that the disease begins in the lower part of the digestive tract. Intravenous alimentation will probably become a more firmly established method also; easy control of nutrition over a deliberately planned rest period is a necessary condition. Miller and Machella emphasize that their advocacy of non-surgical drainage and super-alimentation does not imply that they disregard the possible importance of emotional and infective factors. The work done on the psychological aspects of peptic ulceration does not blind us to the importance of other factors in treatment, neither should similar considerations here prevent a wide appreciation of the problem. The stir made by Bargen's contentions in ulcerative colitis has largely died down but the infective factor must still be considered. The present authors clearly recognize the need for investigation, and where indicated, psychological treatment. Similarly, infection accounts for a number of the serious complications of the disease; wherever the colon is ulcerated there is ample opportunity for bacterial invaders to cause harm. If, however, complete digestive rest can be assured, even without resort to intubation, there would seem good reason to hope that, with other measures like blood transfusion, the patient may be set on the way towards a remission at least.

MEDICAL RESEARCH IN FRANCE DURING THE RECENT WAR.

IN a moving introduction to a book of selected articles translated from the original French into English, and now published in order to show the English-speaking world that medical research continued to exist in France in the last war, Professor Pasteur Vallery-Radot tells of the difficulties facing the conduct of investigation in medical science.[1] "The equipment of laboratories was deficient, often the gas and electricity were cut off . . . . They themselves led a miserable life, underfed, shivering with cold all winter, their minds beset with anguish. They lived under the constant threat of being deprived of their freedom worrying about the fate of their family or friends who were thrown into gaol, deported or shot. How could they be successful in their scientific work? And successful they were . . . They succeeded in performing that herculean task—keeping the French mind alive." Thirty papers embodying the results of true research carried out under these appalling conditions are here presented. It is rather curious when one considers how much surgery owes to France that there should be only one surgical article dealing with "800 lumbar gangliectomies". As the thirty articles have been carefully selected the standard is high and the subjects dealt with cover a wide field in pathology, pharmacology, therapeutics, radio-diagnosis, clinical observation, allergy and the like. Of course here and there a certain "dating" is detectable, but it is of minor importance. For example, Halpern isolated the first of a series of synthetic anti-histamine agents which permitted a guinea-pig to withstand 1500 lethal doses of histamine and discusses the mode of action of these drugs and their probable therapeutic use. The last few years have witnessed a large volume of work, particularly in America, on these anti-histamine drugs, but that does not detract from the value of the original investigation here given. Pierre Blamoutier in a very short but bright article shows that a human being can be sensitized to a product of protein digestion whilst the protein itself gives no positive skin reaction. Lépine of the Pasteur Institute, using an improved ultra-centrifuge, calculates from the rate of sedimentation the size of the bacteriophage. Alajouanine claims to be the first to establish that a great number of sciatic neuralgias is due to a hernia of an intervertebral disk. It would be possible to go through the whole thirty articles, drawing attention to the merits of each and all of them. It is decidedly a book to be read, and the thanks of the profession will be extended to the Rockefeller Foundation for translating and publishing these selected articles showing that the torch of research was kept burning in the darkest years in France's history.

[1] "Medical Research in France during the War (1939-1945): Thirty Articles Gathered and Presented", by Jean Hamburger; 1947. Paris: Flammarion and Company. 10" x 6¾", pp. 306, with many illustrations.

THE SUBCUTANEOUS IMPLANTATION OF INSULIN.

To many diabetics the constantly repeated injection of insulin is a burden that they would gladly lose. Various forms of oral therapy, spurious or well meant, have been put forward, but none have survived. The possibility of subcutaneous implants of an insulin preparation has been considered by a number of investigators, and L. Vargas,[1] who has for some years been conducting appropriate animal experiments with implants, has now published an initial report on the clinical use of the method. He has implanted subcutaneously into seven diabetic patients specially prepared pellets of protamine-zinc insulin and cholesterol, the dose varying from 20·0 to 92·7 units of insulin per kilogram of body weight, except in one exceptional case in which 450 units were given. On the basis of experimental observations in rabbits the daily absorption was calculated to be about 1% of the amount implanted, so that a period of approximately 100 days was covered; this was borne out fairly well in the clinical trials. In the first place control of the blood sugar level was attempted with diet and protamine-zinc insulin so that the daily requirements of insulin might be determined. The daily carbohydrate intake was 90 grammes in one case, 160 to 180 grammes in five cases and 230 grammes in one case. In four cases the injections of insulin were stopped completely after implantation of the pellet; in the other three they were diminished in accordance with previous calculations and with the patient's reaction to the implant. The blood urea content, glycosuria, diuresis and body weight curves were considered in the study of the diabetes. The results in this small series appear to have been quite satisfactory. Apart from the advantage gained in the avoidance of injections there is some evidence that the results obtained are better than with daily injections. This can be understood, Vargas points out, if one remembers that the implant continuously gives out insulin, "imitating the effect of an artificial endocrine pancreas, thus preventing an endocrine disorder and perhaps restoring the pituitary-pancreas relationship". It is, of course, no light undertaking to make this implant with a huge dose of insulin, and previous investigators have frankly regarded it as too risky. However, Vargas seems to have overcome the technical details and it is to hoped that his results can be duplicated by other workers and with larger series of patients.

[1] *The Lancet*, April 9, 1949.

Abstracts from Medical Literature.

SURGERY.

Treatment of Complete Prolapse of the Rectum.

H. T. HAYES AND H. B. BURR (*The American Journal of Surgery*, February, 1948) outline the mechanism of production of rectal prolapse and report on nine cases encountered by them during nine years; three of the patients were subjected to abdominal operation, two by the method of Graham together with construction of a new bed for the sigmoid colon as devised by the authors. They state that rectal prolapse is, as most now agree, a sliding hernia of the anterior rectal wall. This idea was first advanced by Moschcowitz in 1912. The herniation of the recto-vesical pouch or pouch of Douglas occurs through the natural defect in the pelvic fascia that permits passage of the rectum. The enlargement of this defect results from pressure of the contents of the pouch into the anterior rectal wall. The pressure into the anterior rectal wall separates the levators permitting enough anterior rectal wall to be invaginated into the rectum to protrude at the anus. The method of abdominal operation consisted in dividing the peritoneum on each side of the rectum down to and across the pouch and then freeing the rectum as though removal were contemplated. At this stage, instead of suturing the *levatores ani* together as in Graham's technique, the authors sutured the lateral ligaments together in front of the rectum preventing anterior rectal wall from prolapsing through the defect in the *levatores ani*. The cut edge of pelvic peritoneum was turned under and sutured to the rectum at the sides and anteriorly. The lateral peritoneal leaf was then divided from the brim of the pelvis up the lateral gutter for some four to five inches to make a bed for the sigmoid colon, the peritoneal leaf being sutured to the sigmoid colon to hold it in this new bed.

Painful Shoulder.

H. H. HITCHCOCK AND C. O. BECHTOL (*The Journal of Bone and Joint Surgery*, April, 1948) state that lesions affecting the tendon of the long head of the *biceps brachii* are among the most frequent causes of pain and disability in the region of the shoulder joint. The most significant predetermining factors are the presence of the "supratubercular ridge" and a preternaturally shallow bicipital or intertubercular sulcus which, with excessive function or as the outcome of trauma, result in a variety of lesions; these include acute or chronic peritendinitis, varying degrees of attrition and damage to the tendon, and its partial or complete dislocation. The authors found after examining 100 humeri that in 67% of cases the supratubercular ridge was high enough to force the biceps tendon against the roof of the groove and thus cause trauma to the tendon. The fact that pressure against the fibrous roof and inflammatory changes have actually occurred from its presence is proved by the finding of a spur on the lesser tuberosity in the 45% of the humeri which had a supratubercular ridge. Great variation in the depth of the bicipital groove was found. In 8% the medial walls of the groove made an angle of less than 45° and it was considered that in these cases the biceps tendons were dislocated in a fascial sling from a shallow groove. The authors discuss the movement of the humerus in relation to the tendon and the effect of the presence of adhesions. The most constant physical finding in the diagnosis of a lesion affecting the long head of the biceps muscle is tenderness over the tendon. In order to distinguish between peritendinitis and dislocation of the tendon, whether complete or incomplete, the following test is used. After full abduction of the shoulder, the arm which is held in complete lateral rotation is slowly brought down to the side in the plane of the scapula. A palpable or even audible, and sometimes painful click, is noted as the biceps tendon, now forced against the lesser tubercle, becomes dislocated from the groove. The authors point out that peritendinitis of the long head may be associated with other lesions about the shoulder, such as rupture of the tendon of the supraspinatus. If symptoms fail to respond to conservative treatment, such as heat and exercises, the authors advise resection of the portion of the tendon lying above the transverse humeral ligament and suture of the distal portion of the tendon beneath an osteo-periosteal flap made in the floor of the bicipital groove. The shoulder is then put through a full range of movement. Commencing ten days after operation the arm is put through a full range of movement three times each week. The authors have found that loss of pain and the rapid return of function have been characteristic. The only residual disability is slight loss in the power of abduction when the arm is in lateral rotation.

The Management of Acute Circulatory Failure in an Injured Limb.

D. Ll. GRIFFITHS (*The Journal of Bone and Joint Surgery*, May, 1948) states that complete arrest of the arterial circulation of an injured limb is seldom recognized until too late. The mnemonic list of "pain, pallor, paralysis and pulselessness" is usually present in greater or lesser degree. There are four principles of treatment, the first two being applicable in every case, namely, removal of any possible external pressure and restoration of the patient's general condition; if these measures fail to relieve the circulation in the injured limb, and they usually do fail, the surgeon must proceed to the third and fourth principles, operative exposure of the site of obstruction, with appropriate action, followed by post-operative management which is perhaps no less important than the operation itself. At operation under a general anæsthetic only one attempt should be made to reduce fracture by manipulation; if this manipulation fails to improve circulation open reduction is at once indicated. The author recommends exposure of the main artery a short distance above the obstruction and then an arteriogram. The next step is usually to make a generous exposure of the centre of occlusion unless such exploration is clearly too late, that is, beyond twelve hours. The time factor is of particular importance in the case of tourniquet accidents. A tourniquet which has occluded a thigh for six or more hours should not be removed at all, but should be amputated with the limb. If arteriograms show that blockage is distal to the popliteal artery it is wiser not to attempt to relieve the obstruction by open reduction because of danger of diminishing collateral circulation. When there is no contraindication, the occluded vessel is released and widely exposed. Reparable lesions should be repaired. The badly contused or irregularly lacerated vessel, or the artery which shows evidence of intramural rupture should be treated by resection of the damaged portion. For the artery which is found to be intact and apparently undamaged, but tightly occluded by widespread spasm, all possible conservative measures for the relief of spasm should first be attempted. The author states that wide mobilization of the vessel has had success. If it fails, procaine should be injected around the vessel and even into the lumen. The other limbs may be treated by immersion in hot water. Arteriectomy should not be considered unless there is a visible local lesion. If arteriectomy is deemed necessary for any lesion, or if operation results in anything short of full restoration of the circulation, the sympathetic supply of the limb should be interrupted by sympathectomy or paravertebral injections of procaine. The author states that the first few post-operative hours are critical. The systemic blood pressure must be maintained and the limb should be slung on some "open" form of splintage. The limb should be elevated just above the level of the heart and it should be kept cold but not iced. The rest of the body should be heated, even until the temperature rises to 100° or 101° F.

The Effect of Sulphathalidine on Bleeding Time.

L. T. WRIGHT, F. R. COLE AND L. M. HILL (*Surgery, Gynecology and Obstetrics*, February, 1949) record their observations of the bleeding and clotting time of 71 patients and state that these times were increased when sulphathalidine was administered in therapeutic doses. The administration of vitamin *K* reduced this prolongation in most cases. The authors consider that all patients who receive sulphathalidine pre-operatively and post-operatively should, at the same time, receive vitamin *K*.

Gumma of the Lung.

C. W. FINDLAY, W. L. LEHMAN AND L. A. ROTTENBERG (*Annals of Surgery*, February, 1949) report a case of gumma of the lung and refer to the rarity of the condition. The patient was first treated with penicillin and then by resection of the diseased lobe. The result was satisfactory. A rationale is presented for the surgical treatment of pulmonary gumma.

Vaginal and Ovarian Metastases from Hypernephroma.

K. H. MARTZLOFF AND C. H. MANLOVE (*Surgery, Gynecology and Obstetrics*, February, 1949) report a case in which bleeding from vaginal metastases was the first symptom of an unsuspected left renal hypernephroma. They believe this to be the twenty-third case reported of vaginal metastases complicating hypernephroma. They state

that the complication is generally limited to tumours of the left kidney, although exceptions are reported. All patients with hypernephroma complicated with vaginal metastases whose ultimate fate is known died as the result of the hypernephroma, with the exception of those who died at operation. The authors support the view that metastases ordinarily occur via venous channels. Communication of the left ovarian vein with the left renal vein proximally and the pampiniform plexus and utero-vaginal plexus distally explains the peculiar predilection for vaginal metastases to occur with tumours of the left kidney. The suggestion is offered that if the venous theory of dissemination is correct, then left testicular metastases should occur in men afflicted with a left hypernephroma, and would be recognized if looked for. The analysis also suggests to the authors that when a hypernephromatoid vaginal metastasis is diagnosed in a patient who shows no other demonstrable or conclusive evidence of renal tumour, exploration of the left kidney is logical and justified.

The Masking of Inflammatory Processes by Antibiotics.

A. R. CURRERI, E. R. SCHMIDT AND J. T. MENDENHALL (*Archives of Surgery, October, 1948*) point out that, while antibiotics are of inestimable value in the control and treatment of infection, they place on the doctor a grave responsibility, for when complications develop the classical clinical picture is masked, and therefore requires the best possible judgement for its appreciation. Eight case histories are quoted to illustrate this.

Calcium Metabolism in Patients with Spinal Cord Injuries.

L. W. FREEMAN *et alii* (*Annals of Surgery*, February, 1949) review their clinical experiences with over 700 paraplegic patients who had suffered injury to the spinal cord and make special reference to calcium metabolism. They found that the incidence of urinary tract calculi approximated 23% to 35% during prolonged recumbency. They state that ambulation reduced the incidence of calculi to such a degree that the presence of a calculus can be taken as an indication of the failure to arrange sufficient ambulation. Neurogenic ossifying osteomyelitis is discussed as a reflection of the aberrant state of calcium metabolism in the presence of infectious and inflammatory processes.

Fistulæ from Diverticulitis of the Colon.

L. H. MAYFIELD AND J. M. WAUGH (*Annals of Surgery*, February, 1949) discuss 17 cases of sigmoido-cutaneous fistula due to diverticulitis of the sigmoid colon. In each case segmental resection of the colon was carried out. Characteristically the excised segment of colon presented many diverticula. The wall of the bowel was involved in a chronic extramucosal proliferative inflammatory process. Commonly areas of necrosis, abscess formation and perforation were seen. Fistulæ were more common in older than in younger men. The symptoms were the presence of the fistula, abdominal pain, constipation, chills and fever. Each fistula followed some type of surgical operation, usually incision and drainage for an acute suppurative process within the abdomen. These patients had had symptoms suggestive of diverticulitis for an average of approximately 2·5 years when their fistulæ developed. X-ray examination of the colon was the most important aid in diagnosis. Other types of fistulæ were present in about one-third of the cases. The authors state that fistulæ of this type tend to close spontaneously and should be allowed ample time, approximately twelve months, to do so. When surgical treatment is carried out, excision of the diseased segment of colon should be performed and should usually be preceded by a temporary transverse colostomy six months before resection. The choice of procedure depends on the individual case. In the authors' series of 17 cases, 18 segmental resections of colon were carried out with no operative deaths; 16 patients were relieved of their external fæcal fistulæ.

Tendon Repair and Gelatin Sponge.

H. M. NICHOLS (*Annals of Surgery*, February, 1949) presents clinical and experimental data on the use of gelatin sponge in relation to the repair of tendons in the hand and states the following conclusions. The sponge may be placed around a sound tendon without danger and apparently allows earlier free tendon motion. When used about a tendon juncture the sponge causes excessive fibrosis and prolonged fixation of the tendon. Tendon grafts are apparently autolyzed when surrounded by gelatin sponge.

Post-Operative Retention of Urine.

F. K. GARVEY, M. C. BOWMAN AND W. L. ALSOBROOK (*Surgery, Gynecology and Obstetrics*, February, 1949) report the results of treatment with β-methylcholine urethane, a choline derivative, in 76 unselected cases of post-operative functional urinary retention. They state that the drug is stable and causes minimal side actions, which can be completely counteracted by the use of atropine. The drug was successful in relieving the urinary retention in 46 cases and partially successful in 19 cases; in 11 cases the results were regarded as failures. The contra-indications to the use of the drug for post-operative retention are vesical neck obstructions, asthma, hyperthyreoidism, recent intestinal anastomosis, elderliness of the patient (except cautiously in small doses) and coronary sclerosis or known heart disease.

Testosterone Propionate and Breast Cancer.

A. B. MCGRAW (*Archives of Surgery*, September, 1948) reports the use of testosterone propionate in the treatment of twelve patients with breast cancer and from his own and others' experience draws the following conclusions. Testosterone propionate does not cure mammary cancer. Its use as a palliative agent has a logical basis, and its observed beneficial effects when it is so used are such as to encourage further study and use. Its use rather dependably produces subjective improvement, often in pronounced degree and sometimes of considerable duration. Subjective improvement is sometimes accompanied by temporary retardation of bone and skin metastases and occasionally by their regression. The patient in the author's series who responded best were those receiving both a large weekly dose and a large aggregate dose. If maximal individual doses were attained gradually, the initial dose being no more than 50 milligrammes, no undesirable local or general reactions occurred. The best results with respect to duration of palliation were obtained in patients whose metastases had been principally or solely in bone. The authors consider testosterone propionate, used as a palliative agent, to be an adjunct to, not a substitute for, X-ray therapy.

Congenital Pulmonary Stenosis.

ALFRED BLALOCK (*Surgery, Gynecology and Obstetrics, October, 1948*) in the first Rudolph Matas Lecture deals particularly with the technical methods by which the flow of blood to the lungs may be increased and with the anomalies of systemic and pulmonary blood vessels which have been observed by him and his associates during the course of such operations. The three general types of congenital cardiovascular defects which are amenable to surgical treatment are patent *ductus arteriosus*, for which the treatment is obviously closure of the patent ductus, coarctation of the aorta, in which the preferred treatment is excision of the stenotic area and end-to-end anastomosis between the proximal and distal segments of the aorta, and, finally, that in which there is an inadequate pulmonary blood flow and in which mixed venous blood enters the arterial circulation, the most frequently encountered condition of this type being the tetralogy of Fallot. Possible means by which the flow of blood to the lungs could be increased in the tetralogy of Fallot are either an attack on the stenotic area or a "shunt" operation. As the stenotic area is usually in the pulmonary conus of the right ventricle rather than in the pulmonary valve area, excision or incision not only would be dangerous but probably would be followed by a recurrence of the stenosis at a later date. The better procedure is the shunting of some of the improperly oxygenated blood in the aorta to the lungs. The author and his associates have performed anastomoses between (*a*) the proximal end of the right or left subclavian artery and the side of the right or left pulmonary artery, (*b*) the proximal end of the right or left subclavian artery and the distal end of the right or left pulmonary artery, (*c*) the proximal end of the carotid or innominate artery and the side or distal end of the right or left pulmonary artery, and (*d*) the side of the aorta and the side of one of the pulmonary arteries. The type of anastomosis chosen is suited to the case in question. The preferred anastomosis, however, is between the proximal end of the subclavian branch of the innominate artery and the side of one of the pulmonary arteries. The detail of the technique of the procedure is given and the advantages and disadvantages of other procedures are discussed. The author presents a summary as to the type of operation recommended related to the age and size of the patient. Finally an account is given of some anomalies of blood vessels, most of which have been observed in the course of operations, and post-operative care is discussed. The author and his associates have operated on 610 patients with an overall mortality rate of 17·7%.

Congresses.

THE AUSTRALIAN AND NEW ZEALAND ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

THE twenty-seventh meeting of the Australian and New Zealand Association for the Advancement of Science was held at Hobart from January 12 to 19, 1949, under the presidency of DR. A. B. WALKOM, Director of the Australian Museum in Sydney. Part of this report appeared in the issue of April 30, 1949.

Rubella Retinitis.

DR. J. BRUCE HAMILTON (Hobart) read a paper on rubella retinitis and showed a series of slides illustrating changes in the retinæ of deaf children whose mothers had had rubella during pregnancy. An abstract of this paper has appeared in THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, 1948, page 418, and the paper will appear in the *Transactions of the Ophthalmological Society of Australia.*

DR. S. WILLIAMS (Melbourne) asked whether congenital retinitis occurred *per se,* apart from rubella retinitis.

DR. H. MCLORINAN (Melbourne) asked whether the retinæ of these children should be examined as soon as possible after birth; if not, when was retinitis likely to appear.

A speaker asked whether the incidence of congenital defects following rubella had been as high in other parts of the world as in Australia.

DR. F. V. G. SCHOLES (Melbourne) said that he had been interested for many years in the incidence of virus epidemics in different countries. He did not believe in the persistence of a virus between epidemics. He recalled a long gap between epidemics of ordinary measles and had thought at the time that the succeeding epidemic had been started by infection brought from overseas. That had a bearing on the incidence of rubella defects; in Britain and some other countries there was probably no opportunity for young women to grow up without encountering rubella. But just prior to the 1941 epidemic, there were large numbers of young adults in Australia who had never met the rubella virus. It was, of course, possible, as Dr. Hamilton had suggested, that the epidemic had been due to a mutant of the virus.

DR. W. K. MCINTYRE (Launceston) said that it was a pity there was no record of the incidence of rubella during pregnancy. He asked why rubella occurring during pregnancy should not be made notifiable; this would permit of a survey of the true incidence of congenital defects following maternal rubella.

DR. H. MCLORINAN said that the suggestion of such a survey was an excellent one, but he wondered whether it would be possible to carry it out. At present there was a mild epidemic of rubella in Melbourne, and some cases had occurred in pregnant women; but in every instance the patients whom he had seen had insisted, rightly or wrongly, on the termination of pregnancy.

DR. HAMILTON, in reply, said that inherited retinal detachments occurred in association with congenital cystic disease of the lungs. These retinal conditions were definitely inherited, not caused by a congenital infection. In answer to Dr. McLorinan he said that his patients had been examined at intervals of two years. The condition was non-progressive, except in one instance, in which there might possibly have been some progression. As to the age at which examination should be performed, it was not until a child had reached the age of four or five years that a satisfactory examination of the fundus could be performed without a general anæsthetic. Very few instances of rubella defects had been reported in Britain or America. He believed that the epidemics in those countries had been trivial compared with the Australian epidemic. He thought that Dr. McIntyre was quite right to advocate compulsory notification of rubella occurring during pregnancy. In regard to the termination of pregnancy, in his opinion there was not sufficient evidence to justify it at present, even if there were not legal difficulties in the way. In Tasmania there had not apparently been a high incidence of congenital cataract following maternal rubella and the prospects of the deaf children were perhaps not so bad. With the help of hearing aids most could be educated with normal children and could grow up into useful citizens.

Peritonitis.

DR. E. A. HEDBERG (Sydney), in a paper on peritonitis, remarked that there was no condition in surgical practice which provided a better illustration of the struggle between the resistance of the body and the virulence of the infecting organism than peritonitis. The variety of the infecting agents, the complexity of the factors which might modify the outcome, and the mortality of the condition made it an intriguing field for investigation. During the last five years it had caused 2% of the deaths *per annum* at Sydney Hospital. Only one case in fifty occurred without an obvious antecedent; in such instances the patients were usually children. Of the so-called secondary cases of peritonitis, some two-fifths followed appendicitis, one-fifth followed the perforation of a gastric ulcer, and the remainder were associated with a variety of causes. He proposed to discuss certain practical but controversial points in the control of this infection. The first was posture, which had been the mainstay of treatment for many years. When peritonitis was diagnosed, the first step, almost invariably, was to arrange for the Fowler bed, which had been introduced at the end of the nineteenth century by Fowler of New York. Fowler's thesis had been that the pelvic peritoneum could resist infection better than the peritoneum in the upper reaches of the abdomen and that by the aid of gravity infection might be localized in such relatively safe areas. It was probable that at that time—more concerned with morphological than bacteriological considerations—Fowler and his son had been unduly influenced by the favourable outcome of pelvic peritonitis, so often intensely congestive and exudative, caused by the fragile gonococcus. At that time, too, all upper abdominal surgery had been hazardous. MacCallum in 1903 and Cunningham twenty years later had shown that the main route of absorption of particulate matter from the peritoneal cavity was the diaphragmatic peritoneum. Overholt in 1930 had shown that the pressure of the subphrenic spaces varied with the intrapleural rather than the intraabdominal pressures. The negative pressure in the intrapleural space thus aided the upward capillary flow of intraperitoneal fluids. Dr. Hedberg had shown by the use of coloured gelatin solutions administered by intraperitoneal drip that the spread was by thin films between apposed surfaces, and up to the stage when pooling occurred, was independent of gravity, provided the peritoneal cavity was closed. Box in 1910 had said that the peritoneal cavity was a system of watersheds; this seemed to be true only for moderate amounts of fluid, the smaller collections spreading as thin films between surfaces till localized by plastic exudate and the larger overflowing the boundaries of the drainage areas. The delay in the formation of a subphrenic abscess as compared with a pelvic abscess made one ask whether the subdiaphragmatic peritoneum was not every whit as resolute a defender of the body as the lowly pelvic peritoneum. Had posture then any part to play? Dr. Hedberg believed that it had, as long as it was realized that it was employed to favour the accumulations of fluids in regions accessible to diagnosis and treatment. The upright position might well aid respiratory expansion, but the uncomfortable immobility it entailed and the pressure of pillows under the knees and against the feet, enhanced the risk of thrombosis, a significant objection in the elderly. Then, too, the prolapse of distended loops of hypotonic gut might well determine an unfavourable outcome. Dr. Hedberg advocated a position of individual comfort in which regular turning from side to side was possible and which permitted active movements of the legs. Fowler's position, like the tourniquet, was of great value when used with discretion, but was harmful more often than not.

Turning to the resistance of the peritoneum, Dr. Hedberg said that abdominal surgery had advanced *pari passu* with the growth of confidence in the peritoneum's ability to deal with infection. During the last decade the dictum, "When in doubt, drain", had been replaced by, "When in doubt, don't drain". Much attention had been given to means of aiding the remarkable defensive power of the peritoneum. Steinberg, for instance, had devised a preparation called "Coli-bactragen", in which killed coliform bacilli were suspended in tragacanth and aleuronate solution. Injections of that preparation had been shown to accelerate and to enhance the reaction to infection of the peritoneum and omentum. Such work had been largely overshadowed by the tremendous developments in the field of antibiotics. There was no need to elaborate on them, and Dr. Hedberg would therefore pass on to a practical problem not yet solved by the use of such agents, namely, the place of conservative surgery in peritonitis. All were agreed that in the early stages of appendicitis an immediate operation should be done; but in the later stages when a mass was present, it was profitable to try to distinguish the mass which was clearly an abscess and which required drainage from the less tender, usually more diffuse, agglutination of ileum-caecum and omentum about an appendix which might be difficult to recognize and isolate if explored. These required

observant treatment. McNeill Love had shown that 65% of such masses resolved, that 25% formed an abscess, and that in but 10% of cases was a forced operation necessary. Most disagreement occurred about the case of acute appendicitis with diffuse peritonitis. Reports from American workers had shown a remarkable reduction in mortality produced by the deferring of operation in such cases. Despite this the results of immediate operation in early cases of appendicitis with unlocalized peritonitis were so good in experienced hands in Australia that he thought that conservative treatment should be reserved for patients seen after the third day of generalized peritonitis. By that time, in any event, there was usually need for adequate biochemical preparation for operation. At least twenty-four hours should be given to such resuscitation. It had to be remembered that the young, the aged, and the pregnant formed special groups of cases. Recently the conservative treatment of leaking gastric ulcer had been advocated, but instances in which this might be applied were few.

Since general peritonitis was one of the causes of acute hypoproteinæmia, early and adequate replacement of plasma protein was an important part of treatment. Ravdin had said that no considerations of fluid and electrolyte loss and their restitution was sufficient unless protein was simultaneously considered. Dr. Hedberg concluded by saying that the loss of chloride and fluid and the role of intestinal suction and intestinal rest in the management of the distended bowel, which dominated the clinical picture of infection of the peritoneum, would not be discussed by him as they opened up too large a field for his present purpose, which was to be brief and yet to provide sufficient matter for discussion.

Resistance to, and Control of, Infection in Relation to Obstetrics.

DR. A. M. HILL (Melbourne) read a paper on resistance to, and control of, infection in relation to obstetrics. He began by observing that it was only in the previous fifteen years that puerperal infection, which for centuries had been the most important complication of childbirth, had been reduced to a position below that of both the hæmorrhages and the toxæmias of pregnancy as a cause of maternal death and damage. This had been due to a number of factors, of which three were outstanding: an accurate present-day knowledge of the bacterial causes of puerperal infection, a clearer appreciation of the place of maternal resistance in combating infection, and modern chemotherapy.

The mother's general resistance to infection was almost entirely a matter of natural immunity, together with such artificial immunity as she might acquire from inoculation, antitoxin or chemotherapy. The building up of natural immunity began in the earliest antenatal period with: measures directed to the promotion of mental calm and physical fitness; adequate rest and exercise; a full and well-balanced diet, preferably with additional vitamins *A, B, C* and *D*; and the maintenance of the blood hæmoglobin level to as near 90% as possible, if not successfully with diet, then with such aids as iron, hydrochloric acid, and occasionally liver, and blood transfusions. On rare occasions natural immunity might be assisted by an acquired passive immunity. The genital tract of the pregnant woman had a magnificent blood supply and strong anatomical defences against trauma. It also possessed a selective biological immunity against infection by certain bacteria of which such bowel contaminants as *Bacterium coli* and *Clostridium welchii* were good examples. Finally the passage downwards of liquor and blood during labour had a possible cleansing effect. The early diagnosis and treatment of abnormal discharges such as those due to bacteria, *Trichomonas vaginalis* or Monilia was important. In this regard it was worthy of note that Dr. Hildred Butler had found the association of anaerobic streptococci with vaginal moniliasis sufficiently often to suggest potential danger if surgery was contemplated in the presence of Monilia. During labour one could best help the genital tract by minimizing tissue damage and avoiding undue delay in delivery.

Measures to control infection were of two types: those provided by the community and those employed by the obstetrician and his assistants. The communal measures included: the provision of efficient antenatal clinics and almoner services; the housing of the midwifery unit in a separate building with a separate midwifery-trained medical and nursing staff; the presence of "suspect" wards for patients suspected of infection before, during and after labour; facilities for the detection of carriers and for the isolation of patients proved to be infectious; adequate sterilization of all laundry material, including blankets and other woollens; air purification in delivery rooms and nurseries; the oiling of the blankets and floors; and the elimination of dry dusting and sweeping. Individual measures to prevent infection included the building up of the mother's resistance, as already described, and the avoidance or treatment of all infective processes. During labour the essential was an efficient aseptic and antiseptic technique. Attention throughout should be directed to the minimizing of fatigue, tissue damage and blood loss, and each of these should be countered as it arose. Of particular importance was careful management of the third stage, with the utmost reduction of blood loss and rapid replacement when the loss was of undue amount. It needed to be stated repeatedly and with emphasis that if every mother's blood volume and hæmoglobin content were brought to normal levels at the conclusion of labour, the incidence and severity of the common anaerobic infections of the puerperium would be significantly reduced. In the post-natal period the same principles of efficient masking should be applied at each exposure of the vulva and during the dressing of wounds. Prophylactic chemotherapy was the modern contribution to effective prevention. It found its invaluable place in obstetrics in long-standing rupture of the membranes, in cases of prolonged labour, in the presence of a vaginal discharge, or whenever surgical measures were contemplated. The fact and form of its application were determined by bacteriological examinations.

The treatment of puerperal infection was a much later and less important contributor to its control than was its prevention, and Dr. Hill discussed its general features only in outline. He said that successful chemotherapy depended primarily on an accurate bacteriological diagnosis of potential or actual infection, and at the Women's Hospital, Melbourne, the method perfected by Dr. Butler over many thousands of cases was examination of a direct smear, as well as examination, after aerobic and anaerobic culture, of a swab taken from the vagina or, when indicated (as with infection due to *Clostridium welchii*) from the cervical canal.

In conclusion, Dr. Hill emphasized the importance of teamwork between the bacteriological and clinical services devoted to the study and management of puerperal and abortional infections.

DR. HILDRED BUTLER (Melbourne) discussed the relationship observed between severity of infection and the characteristics of the infecting strain in puerperal and abortional infections due to *Streptococcus hæmolyticus* Group A and *Clostridium welchii*.

In a study of 150 cases of infection due to *Streptococcus hæmolyticus* Group A it had been shown that 53 out of 61 strains causing mild infections failed to produce capsules when grown in human blood, whereas all but one of 26 strains associated with severe and fatal infections were heavily capsulated. Of the intermediate group of 63 moderately severe infections, 39 were occasioned by moderately capsulated strains, 12 with uncapsulated variants, and the remaining 12 with strains which were heavily capsulated. In addition, of 87 strains isolated from the blood-stream (in this series there had been some non-puerperal septicæmias), all but one readily produced capsules in human blood.

Dr. Butler said that she regarded these findings as indicating that the severity of infection with *Streptococcus hæmolyticus* Group A depended on the virulence of the infecting strain rather than on variation in resistance from patient to patient.

Similarly in *Clostridium welchii* infections no evidence had been obtained of variation in resistance from patient to patient; severity of infection depended on the pathogenicity of the infecting strain. Only those strains which were heavily capsulated and highly toxigenic were capable of producing severe infections. Such strains had constituted only 3% of the total number of *Clostridium welchii* strains recovered from the genital tract in abortional cases. It had been found possible to assess both the degree of capsulation and the toxicity of a particular strain multiplying in the genital tract by examining stained cervical smears. In the clinically severe infections the cervical smear stained by Richard Muir's method had invariably shown large capsules, and even more important, it revealed that rapid destruction of the leucocytes was taking place (the latter was apparently due to the action of the exotoxins). In cervical smears from the milder infections this combination had not been seen. The combination of heavy capsulation and destruction of the leucocytes had been observed in the cervical smears in all but four of 98 cases of severe infection, but only twice in a series of 207 cases of various types of mild *Clostridium welchii* infection.

In the second half of her paper Dr. Butler gave the results of the examination of stained smears from cervical or vaginal swabs in nearly 20,000 puerperal and abortional cases. This method had proved satisfactory for the detection

of all bacterial types of infection in 80% of cases. Apart from its speed the method had the advantage that in many instances it indicated the probable severity of infection and in the *Clostridium welchii* infections the clinical type also.

Dr. Butler showed case records to illustrate the use of stained smears as a guide to chemotherapy and therefore in the control of infection in the individual case. She referred specially to the value in the mixed anaerobic infections of smears as compared with cultures as a means of determining whether the administration of penicillin or of sulphonamides or both was required for the control of a particular infection. She also stressed the value of serial smears in the assessment of the efficacy of treatment.

DR. M. WILSON (Hobart) commented on the value of the teamwork described by Dr. Hill and Dr. Butler, which had been carried out at the Women's Hospital, Melbourne, since 1934. He asked Dr. Butler whether any special methods were employed in the staining of vaginal smears used in the bacteriological diagnosis of infections.

PROFESSOR S. RUBBO (Melbourne) congratulated the speakers on their lucid and interesting account of the subject. It illustrated a pleasant synthesis of work in this sphere and was a valuable contribution to clinical medicine. He thought, however, that the bacteriological diagnosis of infection from examination of a vaginal smear was not easy for people who had not had Dr. Butler's vast experience. He asked Dr. Butler's opinion on this point.

DR. W. K. MCINTYRE (Launceston) said that he heartily agreed with Dr. Hill's remarks about the minimizing of fatigue during labour and its importance in regard to infection. The overworked housewife who came into hospital worn out and in labour was a type of patient in whom infection was likely to occur. He had advocated the use of bedside X-ray units, to make a check on the position of the child and to prevent unnecessary prolongation of labour. He also deprecated the indiscriminate use of penicillin and sulphonamides without adequate bacteriological diagnosis.

DR. E. S. MORRIS (Sydney) said that in the past he had adopted the attitude that the Group A hæmolytic streptococcus was the only dangerous organism from the point of view of the spread of infection in an obstetric hospital. Did Dr. Hill agree with this?

DR. ARTHUR HILL, in reply to Dr. Morris, said that the only obstetric infections which needed be treated as dangerous to other patients were those due to *Streptococcus hæmolyticus* (Group A) or to *Staphylococcus pyogenes*.

DR. BUTLER, in reply to Dr. Wilson's question about the staining of smears, said that two smears were stained as a routine practice. The first was stained by Gram's method; if streptococci were seen, the smear was overstained by Leishman's stain, which showed up the capsules if any of the streptococci. The second smear was stained by Muir's capsule stain. In reply to Professor Rubbo, she said that diagnosis of vaginal infection by the smear technique presented difficulties in a few cases, but in the majority of instances, a comparatively inexperienced pathologist would be competent to examine such smears. Good cooperation between the clinical and bacteriological staff was important.

Transmission of Infectious Diseases to Marsupials.

DR. A. BOLLIGER (Sydney), discussing the transmission of infectious diseases to marsupials, pointed out that for a period of about one hundred million years the Australian marsupials had remained in a definite state of isolation, and he examined the question whether a typical local marsupial, the common possum or phalanger (*Trichosurus vulpecula*) exhibited any immunological peculiarities inherited from that remote period when it emerged from its reptilian ancestry. He had administered viruses, bacteria and protozoa to this pouched mammal. The viruses employed were those of ectromelia, poliomyelitis, canine distemper, bovine infectious labial dermatitis, chickenpox, pigeonpox and cowpox. The bacteria administered were acid-fast bacilli such as human, bovine and avian *Mycobacterium tuberculosis*. In addition bacilli obtained from lepromata and acid fast bacilli from a skin lesion, recently described as a new infectious disease (MacCallum, Tolhurst, Buckle and Sissons), were administered to phalangers. The protozoa used were *Leishmania donovani, Trypanosoma cruzi, Plasmodium vivax* and *falciparum* and *Entamœba histolytica*. Some of the outstanding findings were a high pathogenicity of *Leishmania donovani*, producing kala-azar in 95% of the inoculated possums. The majority of the infected animals developed eye lesions resembling those seen in human syphilis. Some of the Mycobacteria investigated exhibited a high virulence towards *Trichosurus vulpecula*. This was very marked with bovine strains of *Mycobacterium tuberculosis*. Another interesting finding was that the incubation period for the new mycobacterial disease was several months shorter in the possum than in the rat.

The Pathology of Certain Protozoal Infections in Marsupials.

DR. T. C. BACKHOUSE (Sydney), after referring to Dr. Bolliger's work showing that a variety of human infections could be transmitted to the common Australian possum, went on to give a brief description of the pathology of two such infections. These were due to two members of the family Trypanosomidæ, namely, *Leishmania donovani* and *Trypanosoma cruzi*. In the former infection the reticulo-endothelial system was invaded and responded by gross hyperplasia. There was a secondary plasma cell infiltration. These points were illustrated by photomicrographs of histological sections and emphasis was laid on the plasma cell reaction with special reference to recent work by Fagraeus (1948) in Stockholm, showing the relationship between plasma cell development and antibody production. The chief features of the pathology of *Trypanosoma cruzi* infection were mentioned and illustrated by reference to photomicrographs of tissues of possums infected with this protozoon. It was considered that the possum was a very useful animal for the study of such infections and for extending the knowledge of cellular reactions and immunity phenomena in protozoal and other diseases.

PROFESSOR F. M. BURNET (Melbourne) said that Dr. Bolliger and Dr. Backhouse had established the fact that the possum was a useful experimental animal. The fact that the possum's body temperature varied from 90° to 95° F. interested him because in egg culture of viruses a temperature of 35° C. was much more favourable for growth than the physiological normal. An attempt should be made to use the possum in virus work. He had been interested in the presence and type of plasma cells in the sections shown by Dr. Backhouse. They were very like those described in a very interesting monograph by Fagraeus. A study of these large immature plasma cells should add interest to the histological study of many inflammatory lesions. He asked whether any work had been done to show that the possum was a good producer of any common type of antibody.

DR. I. M. MACKERRAS emphasized the importance of gathering in new experimental animals. In Queensland they hoped that a survey of marsupials would be made in the near future; especial attention would be paid to their possible use as experimental animals. He commented on the amazing intensity of the cellular reaction in the slides shown by Dr. Backhouse. One very interesting thing in the pathology of kala-azar was the amazing way it revealed the macrophages of the reticulo-endothelial system. This was particularly noticeable in sections of skin. Kala-azar was a most interesting condition, the study of which would be much helped by these experiments on a new host.

DR. BOLLIGER, in reply to Professor Burnet, said that he knew of no work on the production of antibody by the possum. In reply to Dr. Mackerras, he said that he realized that the possum was only one of many animals native to Australia which might be used in experimental work. He was trying to find a smaller suitable animal, and had found that the kangaroo rat stood up to laboratory work very well.

(To be continued.)

British Medical Association News.

SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held on December 15, 1948, in the Verco Theatre of the Institute of Medical and Veterinary Science, Adelaide, the President, DR. A. D. LAMPHEE, in the chair.

Recent Developments in Urology.

DR. NOEL J. BONNIN read a paper entitled "Recent Developments in Urology" (see page 612).

DR. I. B. JOSE said that he was interested in what was said about infections of the urinary tract; he considered that streptomycin was going to be of great assistance in infections which could not be controlled by sulphonamide drugs or penicillin. Regarding tuberculosis of the renal tract he believed that it was generally considered that once a caseating lesion was present streptomycin did not have a

very great effect, but it was interesting to hear from Dr. Bonnin the account of such a successful result in the case he had described. Probably the greatest benefit would be in the type of case in which a nephrectomy had been performed, but tubercle bacilli were still present in the urine. "Moogrol" and other drugs would probably also prove to be of assistance. Uneradicated renal tuberculosis had always been a slowly progressive relentless disease. Dr. Jose then inquired if Dr. Bonnin had had any reference to the local use of streptomycin in the bladder for tuberculosis. A patient whom he had treated by ionization with a solution of streptomycin had done very well. Dr. Jose said that he was interested in the classification of tumours of the testicle described, and was particularly interested to hear that the Americans were again using radical removal of the lymph glandular drainage area in certain types of tumour which were not sensitive to deep X-ray therapy. Regarding prostatectomy, Dr. Jose said that there was always tremendous variation in the method of attack on the prostatic condition. Possibly the Terence Millin method would be the one favoured by the younger school of surgeons, but it was necessary to be practised and skilled in one method. If a surgeon could become a good resectionist then he had a good method for a great number of cases. The average surgeon or urologist considered that for some types of prostatism resection was the only method. With regard to mortality, in most cases the patient died of embolus and that would occur whatever method was used. The other cause, namely, infection, should be controlled at the present time. The days of long catheterization were over. With regard to the treatment of carcinoma of the prostate, it was interesting to hear the diverse views on the dosage of œstrogens; he asked Dr. Bonnin if a definite cure by that form of treatment had been reported.

DR. G. H. BURNELL said that with regard to pyelonephritis he had always had difficulty in deciding when the kidney was infected. Possibly that difficulty was associated with the use of ureteric catheters sterilized by formalin vapour. He asked Dr. Bonnin what was the common method of sterilization of ureteric catheters used in the United States. He was also interested to hear of streptomycin and "Moogrol". Using those drugs he had had one dramatic cure in a very short time of a suprapubic fistula from a tuberculous bladder. Dr. Burnell said that he did not think that many patients with bilateral calculi showed evidence of hyperparathyreoidism. He had only seen two proven cases and had been looking out for the condition for many years. He had just operated on a patient that day who had bilateral calculi, and had removed three tumours from the thyreoid, but the reports of the pathologist were not yet to hand. He also said that he was disappointed with the results of the use of solution G. for renal calculi. For one thing it was necessary to be sure that it was a phosphatic calculus that one was trying to dissolve. With regard to preoperative tests in prostatic operations, he agreed that less respect was being paid to tests of renal function, but more notice was being taken of infection. He did not hesitate to operate in the majority of cases, provided that the urine was uninfected, but he was becoming more and more cautious about operating in the presence of infection. The "Latex" catheters, he considered, were good and probably did not set up so much urethritis as the red rubber catheter, but he found it difficult to suck out a "Latex" catheter if it became blocked with pus or blood, as the walls were soft and collapsed with suction. He had had good results with ordinary red rubber catheters after treatment with silver nitrate by a special method. The Millin operation, he considered, was a difficult operation. He had performed it in 81 cases with four deaths, two from embolus, one from operative shock and one from coronary disease. One patient had developed *osteitis pubis*. He was disappointed with œstrogenic treatment of carcinoma of the prostate. The first patient on whom he had tried this therapy lived six years, but he had not had such a good result since. He found that the patients progressed fairly well for about three years and then went downhill. In some cases there was definite retrogression of the prostatic tumour, and in other cases the gland remained hard and fixed. There seemed to be two types of carcinoma of the prostate from that point of view. He had tried podophyllin in several cases. It certainly had had a destructive effect on papillomata, but it was too early to express any definite opinion.

DR. A. LENDON asked Dr. Bonnin if he had seen any of the devices for the extraction of ureteric calculi. In regard to malignant disease of the testis, he asked if there was any improvement in prognosis when block dissection of the glands was used.

DR. J. CLOSE asked if Dr. Bonnin had seen any patients with anuria treated by peritoneal lavage. With regard to carcinoma of the prostate, he stated that the statistics of the past ten years at the Royal Adelaide Hospital were very depressing reading. He wondered whether the general usage of œstrogens might have caused the patients in a few of the early cases to miss their chance of cure by radical surgery. In regard to hyperparathyreoidism his own experience was that usually all the clinical tests failed to prove anything, and he wondered whether in such cases of multiple renal calculi the patient should have surgical treatment when the clinical findings were negative.

DR. IAN HAMILTON discussed prostatic surgery. He said that in New South Wales it appeared to depend on the school to which one belonged whether endoscopic resection or the Harris method was used, but he did know of patients who had undergone a suprapubic operation when a resection had previously been performed. Some time previously he had read an article on prostatectomy in which the surgeon advocated operation as soon as possible when a patient was admitted to the ward with acute retention of urine; he quoted personal illustrations of cases in which that procedure had considerably shortened the patient's stay in hospital and also avoided infection of the patient's urinary tract by preliminary treatment while he was awaiting a routine operation. Dr. Hamilton also asked Dr. Bonnin whether it was true that the sale of incontinence clamps had gone up tremendously since the endoscopic operation had become popular.

In reply to Dr. Jose, Dr. Bonnin said that he had not seen streptomycin used locally. In the United States there was a good supply of streptomycin, and tuberculosis of the renal tract was regarded and treated as a generalized disease, so that parenteral administration was preferred. He said that œstrogen treatment of carcinoma of the prostate was usually effective only for a time and then recurrence of symptoms took place. In some cases the condition did not seem to respond much at all. In a few cases, however, the growth appeared to be controlled for a very long time and Dr. Bonnin felt that there might be some chance of a cure. In cases in which relapse occurred it was worth trying large doses of œstrogens and it might be worth trying luteinizing hormones or X-ray therapy to the pituitary. In reply to Dr. Burnell, Dr. Bonnin said that the method of sterilizing ureteric catheters which he had seen used in the clinics he had visited had been by means of a watery solution of antiseptic, usually mercurial. The catheters were fixed with one end in a dish of the antiseptic and the solution was allowed to siphon through the catheters for a number of hours. This was followed by a thorough wash with sterile water. He had not seen the formalin cupboard used in the United States. With regard to the rapid healing of a fistula from a tuberculous bladder reported by Dr. Burnell, Dr. Bonnin said that streptomycin was characterized by a rapid lethal effect on organisms. If organisms survived the first blow they quickly developed a high degree of resistance. It was a similar sort of rapid healing of a tuberculous lesion in a ureter which might suddenly produce a stricture during streptomycin therapy of renal tuberculosis. In reply to Dr. Lendon, Dr. Bonnin said that ureteric instruments which engaged a stone and would not disengage it were regarded as rather dangerous. The more popular special instruments seemed to be the Balkus looped catheter and the Dourmashkin bag. He demonstrated a Balkus catheter. Dourmashkin bags were very fragile and did not keep well in storage, and it was considered that travel through the tropics would not improve them. He could not quote any figures comparing the results of radical operation with simple orchidectomy, but he believed that in the group of carcinomata the prognosis was improved by the radical operation. With the trophoblastic tumours the prognosis was almost hopeless, so that not much improvement could be expected with that group. The radical operation was not usually performed for the X-ray sensitive seminomata, as there was little to be gained by the procedure. In reply to Dr. Close, Dr. Bonnin said that he had intended to discuss briefly the management of anuria, but time had not allowed it. Peritoneal lavage was reserved for the time when the patient began showing definite signs of uræmia. The continuous perfusion method was usually employed. A carefully prepared solution was used and administration had to be carefully controlled. It was effective for about three days. Thereafter, the efficiency of dialysis declined as the peritoneal cavity became shut off by adhesions, the dializing surface thus decreasing. After the third day there was a real risk of bacterial peritonitis. In regard to carcinomata of the prostate, a few patients might have missed a chance of cure, but they would not be many; of 1961 patients at Baltimore, only 2·7% had been given a five-year cure by surgery, and in the Brady Institute not many operable growths would have been missed. In reply to Dr. Hamilton, Dr. Bonnin said that in the early days of resection when large numbers of people bought resectoscopes

and tried the operation there was undoubtedly a large increase in the sale of clamps. However, when the operation was carried out by a skilled resectionist the risk of incontinence was very small indeed. There might be some risk in cases of carcinoma in which the external sphincter was infiltrated by the growth.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Course in Advanced Medicine.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a course in advanced medicine suitable for M.R.A.C.P. candidates will be conducted for a period of fifteen weeks from June 6 to September 16, 1949. Fees for attendance will be £39 7s. 6d. or £2 12s. 6d. per week. The programme has been arranged to take place almost exclusively in the afternoons from approximately 2 p.m. to 5 p.m. on five days per week and will include: (*a*) Didactic lectures on the more obscure aspects of internal medicine, designed to supplement the students' reading. These will cover the various systems in turn. (*b*) Lectures and tutorials in electrocardiography. (*c*) Ward rounds and demonstrations of cases at the principal metropolitan hospitals approximately twice weekly. (*d*) Regular clinico-pathological conferences. (*e*) Demonstrations of the *fundus oculi*. (*f*) Lecture-demonstrations in physiology and biochemistry and discussions on applied physiology. (*g*) Lecture-demonstrations in pathology and hæmatology. (*h*) Demonstrations of the application of radiological methods of diagnosis to medical diseases. (*i*) Demonstrations of psychiatric cases. (*j*) The exhibition of selected medical films.

The supervisor of the course will conduct tutorials on selected subjects and students may discuss with him any problems arising in the course of their work. It is expected that candidates will devote a considerable time to general reading, both of text-books and current medical literature. The object of the course is to provide assistance and guidance for the serious students of internal medicine. It is desirable that students should have had considerable clinical experience in hospital and/or in medical practice before considering themselves prepared to take examinations for higher medical degrees or diplomas.

Fees are payable in advance at enrolment date and applications to attend whole or portion of this course should be in the hands of the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, no later than May 27, 1949.

Course for Diploma in Dermatology.

A Part I course for the Diploma in Dermatology of the University of Sydney will begin in Sydney on June 20, 1949, for a period of twelve weeks. After a vacation of two weeks, a Part II course will begin in September and will continue until about a month before examinations begin in April-May, 1950.

Copies of the by-laws and regulations governing this diploma may be obtained on application to the committee's office and early enrolment should be made to the Course Secretary of the committee, 131 Macquarie Street, Sydney.

Week-End Course at Katoomba.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course will be held in conjunction with the Blue Mountains Medical Association in the lecture room of the Blue Mountains District and Anzac Memorial Hospital on Saturday and Sunday, May 21 and 22, 1949. The programme is as follows:

Saturday, May 21.—1.45 p.m., Registration; 2.15 p.m., "Pædiatric Problems", Dr. Lorimer Dods; 3.50 p.m., "The Present Position of Vascular Surgery", Dr. Frank H. Mills.

Sunday, May 22.—9.30 a.m., "Pædiatric Problems", Dr. Lorimer Dods; 11.10 a.m., "Placenta Prævia", Dr. H. Bruce Williams; 2.15 p.m., "Thiouracil in Thyreoid Disease", Dr. Frank H. Mills; 3.50 p.m., "Obstetric Difficulties", Dr. H. Bruce Williams.

The fee for attendance is £2 2s., and those wishing to enrol are requested to notify Dr. Nicholas Larkins, Honorary Secretary, Blue Mountains Medical Association, 199 Katoomba Street, Katoomba, at an early date.

Special Correspondence.

NORTH AMERICAN LETTER.

FROM OUR SPECIAL CORRESPONDENT.

WARTIME and post-war migration has brought the population of the State of California up to ten million. As a result hospitalization is becoming an almost insoluble problem. Despite this there are many bills before the California State Legislature concerning tax-supported medical care and hospitalization schemes which threaten to compound the local difficulties further. Almost one-tenth of the 4701 bills brought before the Legislature concerned public health matters in one form or another. The chief bill is one on compulsory health insurance sponsored by the Governor. On two previous occasions this bill failed to get to the House floor because of failure to win approval in committee. It will be interesting to see its course in the near future, as it offers such benefits as one hundred days of hospitalization, including medical care, for what the Governor calls "catastrophic illness"—a term nowhere defined in the bill. All medical and hospital benefits are to be financed through a 1% tax on the first $3000 of income earned, and a similar tax on employers. Medical care would be restricted, in the Governor's bill, to that provided by medical doctors and osteopaths. The American Federation of Labor, however, has a rather parallel bill, in which they would open the scheme to chiropractors as well. Their plan calls for 21 days of free hospitalization. One of the bills makes it illegal for a doctor to charge any fee, in addition to what the insurance fund awards him, to a patient earning less than $6000 per year. The burden of proof of income status seems to be on the doctor, and if he finds, too late, that he has charged an added fee to a person earning less than $6000 he is likely to have his licence revoked.

No rates of payment are specified in the bills, but the benefits are really all-inclusive, with X-ray, laboratory and dental services supplementing the medical and hospital care. The scheme is to be administered by an authority, of ten members, with the Director of Public Health for the State as chairman. The head of the Department of Employment will be on the commission (without a vote), *plus* three physicians, one of whom must be experienced in hospital administration, two employers, two employees, and one dentist. All these persons will be appointed by the Governor.

There is a provision in the bill for the spending of from $700,000 to $900,000 per year for the post-graduate training of practising physicians. Christian Scientists will be exempt, as will farmers, domestic employees, self-employed and Federal Government employees. Services not covered are the office or home visits of the physician prior to hospitalization of the patient, the cost of two days' hospital care except in surgical or obstetrical cases, and first $10 of laboratory or X-ray services. The administrative costs of the scheme are limited to 6%.

Voluntary plans which offer the same range of services for the same cost to the patient will be allowed to cover employees and families, provided that a majority of employees in an establishment vote for it.

A separate bill has been introduced to curb the pernicious practice of rebates in this State, which may serve to prevent recipients of "free drugs" at some time in the future cashing in prescriptions *et cetera*.

It should be emphasized that Governor Warren of California was vice-presidential candidate on the Republican ticket with Thomas Dewey, and in no way reflects the Roosevelt-Truman New Deal political philosophy. Possibly, therefore, the fact that he sponsors such a bill as outlined above will serve to show what the public temper is in medical matters in the United States.

In Canada the chief topic of medical conversation is the enormous grants which the Federal Government at Ottawa is making to approved schemes in each of the provinces. Programmes of unparalleled dimensions in the Dominion's history are being transfused from the Treasury at Ottawa, which has retained many of its wartime taxation fields. Half a million dollars have been set aside annually for professional training of people to implement these programmes in the fields of cancer, mental hygiene, venereal disease, tuberculosis and most importantly the rheumatic diseases. In many cases the funds are dispensed to lay and professional groups which have combined to fight these diseases. Because of the variation in local conditions and local needs, no stereotyped programme has been superimposed on the country, but regional responsibility and pride in local undertakings have been stimulated to the full.

The College of Physicians and Surgeons of British Columbia has recently entered into an agreement with the Provincial Government whereby the profession as a body has undertaken to provide complete medical care for all persons in receipt of "social assistance", or "relief" as it was once called. The profession receives $14.50 per person covered, and this is pooled by them. The entire administration of the plan lies in medical hands, and the success of the undertaking is the responsibility of the College. They will discipline physicians if required, survey all bills *et cetera*. The fees to be charged within the system are the minimum fees of the College. This experiment of a medically run plan carried out at government request for the benefit of those who are truly "medically indigent" will be worth following, and its course will be described later in these letters.

Correspondence.

THE PETROL TAX.

SIR: This tax was initiated in 1926 at the rate of threepence a gallon of petrol for the construction and maintenance of roads. It seemed in those distant and more rational times not an unreasonable move. Motorists as a class were shocked to find that they were regarded as able to find an additional fourpence in 1930 to offset the loss of revenue during the depression, and our profession, always large users of petrol, was hit as hard as any, but in 1940 a further amount of threepence halfpenny was added to meet war expenditure. The reasons for the last two impositions have long ceased to exist.

Generally governments appreciate the value of roads in development. Ours has been content to leave 278,000 out of 489,000 miles of roads unimproved. They have diverted £8,671,407 out of 1947-1948's £16,009,515 collected from petrol tax (in effect) to general revenue. This is being done in spite of their cry for more and more production. But bad roads increase maintenance, handling, wear and tear on vehicles and goods, time in transit, and in wages and petrol used. The burden of the tax is unfairly distributed on the producing section of the community and made worse by the uneconomic policy of the Government.

Two courses appear possible: firstly to abolish the tax and cause the burden of road upkeep to be spread over the whole population of taxpayers, or secondly to devote the entire sum ostensibly collected through the petrol tax to much-needed road improvement.

Yours, etc.,
J. M. DWYER.

Hindmarsh,
South Australia,
April 13, 1949.

MEDICAL EDUCATION IN AUSTRALIA.

SIR: In your leading article on January 10, 1948, you recommended that attention be given to the subject of medical education in Australia, and stated *inter alia* that "Australia cannot sit back and wait until Britain, Canada, or America has solved a problem from the British, Canadian, or American point of view and apply the solution to its own needs".

Your leading article further stated that the Federal Council should do something to set an inquiry going into this problem from the Australian point of view.

It is interesting to read in *The Journal of the American Medical Association* (December 4, 1948) that a survey of medical education is now being carried out in the United States of America. This is the third survey in forty years, the first being the well-known one by Abraham Flexner. The present survey is being sponsored by the Council on Medical Education and Hospitals of the American Medical Association, and the Association of American Medical Colleges.

It is unfortunate that we have no bodies corresponding to these in Australia.

From time to time suggestions have been made that there should be a uniform matriculation examination for entry into the various Australian medical schools. In connexion with this suggestion a recommendation was made some little time ago that a medical officer should be appointed to act as a liaison officer between the various Australian Faculties of Medicine, so that each would be well informed of the activities of the others.

In America a director of the survey of medical education has been appointed, and to help him there is a committee consisting of seven members.

Inquiry is to be made into the following matters:

(1) Improving medical education to better meet the overall needs of the American people.
(2) Assessing the degree to which medical schools are meeting the need of the country for physicians.
(3) Promoting the advancement of knowledge in the field of medical science.
(4) Better informing the public concerning the nature, content and purposes of medical education.

Many sound reasons can be given in support of your recommendation for a survey of Australian medical education.

Yours, etc.,
E. S. MEYERS.

The University of Queensland Medical School,
Herston Road,
Brisbane, N.1.
April 18, 1949.

A NATIONAL MEDICAL SERVICE.

SIR: In the controversy about the nationalization of medical services, why does no one trouble to investigate the Northern Territory Medical Service? The Northern Territory is in its fourth year of "free" medicine, and is now boiling over with public discontent.

The Northern Territory Medical Service is completely controlled by the Commonwealth Department of Health, a department which has failed so utterly and wretchedly in the Northern Territory that it can hardly by any stretch of imagination be held likely to succeed over the whole of Australia.

Last February a select committee of the Northern Territory Legislative Council expressed "the gravest concern" at evidence given before it of "medical crimes" and "general maladministration", and recommended a thorough and impartial inquiry into the Northern Territory Medical Service.

As medical officers in that service we feel that a full investigation into the four years of nationalized medicine in the Northern Territory would result in a betterment of medical services and would bring home to the people of Australia just what to expect from a nationalized service.

Yours, etc.,
JACK SUNDERMAN, Medical Officer-in-Charge, Katherine Hospital; V. H. WEBSTER, Medical Officer-in-Charge, Tennant Creek; R. M. WITHERS, Medical Officer, Darwin Hospital.

Northern Territory,
April 20, 1949.

Public Health.

THE POLICE OFFENCES (AMENDMENT) ACT, 1908, OF NEW SOUTH WALES.

THE *Government Gazette of New South Wales* for April 29, 1949, contains the following regulation in connexion with the *Police Offences (Amendment) Act*, 1908.

His Excellency the Governor, with the advice of the Executive Council, and in pursuance of the provisions of the *Police Offences (Amendment) Act*, 1908, as amended, has been pleased to amend the Regulations made thereunder in the manner set forth hereunder.

J. M. BADDELEY.

The Regulations are amended by *adding* after Regulation No. 15 the following new heading and Regulation:

Possession and Use of Drugs in Aircraft.

15A. (1) A person licensed by the Director-General of Civil Aviation to engage in regular public transport operations is hereby authorised to be in possession of morphia and morphine-like substances for installation in aircraft so far as is necessary for the purpose of complying with the requirements of any Regulation or Order in pursuance of the Commonwealth Air Navigation Act, 1920-1947, subject to the following conditions:

(*a*) That the drugs are stored in a sealed first-aid kit in the aircraft.

(b) That the drugs are used only for emergency purposes.

(c) That any such drugs installed in an aircraft shall not exceed the quantity required to be provided in the scale of emergency equipment prescribed under the abovementioned Regulations or any Order issued thereunder.

(2) The first-aid kits in which the drugs are stored shall be inspected periodically by a medical officer or some other responsible person appointed for the purpose and, when practicable, as soon as possible after a kit has been used in an emergency.

(3) A person authorised under this Regulation to be in possession of drugs for installation in aircraft shall make provision for a medical practitioner or approved person to enter or cause to be entered in a register kept solely for that purpose under the provisions of Regulation 11 a record of—

(a) all supplies of the drugs purchased or otherwise obtained by him;

(b) all quantities of the drugs issued by him, together with the designation number or letters of the aircraft in which the drugs are to be stored;

(c) the date and place in which the drugs were used for emergency purposes on any particular aircraft, and the quantity so used.

(4) The holder of a licence to manufacture or distribute drugs or any person authorised under the Regulations to dispense drugs may supply drugs pursuant to paragraph (1) of this Regulation on the written order of a medical practitioner appointed by the person authorised to be in possession of such drugs or if a medical officer has not been so appointed on presentation of the written order of such person endorsed by the Superintendent of Aviation Medicine, Department of Civil Aviation.

(5) The Captain of an overseas aircraft engaged in public transport operations which is in the State of New South Wales is hereby authorised to be in possession of such quantity of the drugs mentioned in paragraph (1) of this Regulation as may be certified in writing by the Superintendent of Aviation Medicine, Department of Civil Aviation, to be necessary for the equipment of the aircraft. The holder of a licence to manufacture or distribute drugs or other person authorised under the Regulations to dispense drugs may supply any drugs in accordance with such certificate.

(6) A person who supplies a drug in accordance with a certificate or order given under this Regulation shall cancel such certificate or order and retain it on a special file for a period of not less than two years.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Acts*, 1939 *to* 1946, of Queensland, as duly qualified medical practitioners:

Crowther, Geoffrey Earl, M.B., B.S., 1936 (Univ. Sydney), Hospitals Board, Isisford.

Mackerras, Mabel Josephine, M.B., 1924 (Univ. Sydney), Nelson Street, Corinda.

Maclurkin, Iver Douglas Macarthur Brodie, L.R.C.P. and S., 1938 (Univ. Edinburgh), L.R.F.P. and S. (Univ. Glasgow), Taroom.

Silberstern, Ernest, M.B., B.S., 1946 (Univ. Sydney), Westwood Sanatorium, Westwood.

Zamel, Jack, M.B., B.S., 1946 (Univ. Sydney), Hospitals Board, Atherton.

Medical Prizes.

THE DAVID ANDERSON-BERRY PRIZE.

A DAVID ANDERSON-BERRY SILVER-GILT MEDAL, together with a sum of money amounting to about £100, will be awarded in 1950 by the Royal Society of Edinburgh to the person who, in the opinion of the Council, has recently produced the best work on the therapeutic effect of X rays on human diseases.

Applications for this prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of relevant papers.

Applications must be in the hands of the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh, 2, by March 31, 1950.

Diary for the Month.

MAY 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
MAY 12.—Victorian Branch, B.M.A.: Organization Subcommittee.
MAY 13.—Queensland Branch, B.M.A.: Council Meeting.
MAY 16.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
MAY 17.—New South Wales Branch, B.M.A.: Medical Politics Committee.
MAY 18.—Western Australian Branch, B.M.A.: General Meeting.
MAY 19.—New South Wales Branch, B.M.A.: Clinical Meeting.
MAY 19.—Victorian Branch, B.M.A.: Executive Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135 Macquarie Street, Sydney): Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester United Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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